Medically Unexplained Symptoms in Neurology

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ABSTRACT OF THESIS

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Title of Thesis- Medically Unexplained Symptoms in Neurology.

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Aims- To estimate the proportion of new patients with medically unexplained symptoms (MUS) that present to neurology out-patient services and to examine the impact of such symptoms on the patients in terms of disability, distress and outcome.
Methods- Historical (MUS from 2 000 BC to 1965), narrative (non-neurological MUS) and systematic (MUS in neurology 1960 – 2000) reviews of the previous literature were conducted. A prospective cohort study of 300 newly referred out-patients was carried out in the regional neurology service in Lothian, Scotland. Patients were examined at the time of initial presentation and re-examined eight months later. Both primary and secondary care case-note were reviewed at follow up.
Measures- Neurologists rated degree to which the patients' symptoms were explained by organic disease. Health status was measured using the SF-36. Anxiety and depressive disorders were examined using the PRIME MD and HAD. Outcome was measured on a Clinical Global Improvement (CGI) scale.
Results- The historical review of the literature found that MUS have been described since the first written texts of medicine. The narrative review showed that MUS affected both sexes, all ages, and all cultures. The systematic review of MUS in neurology found that between 30-40% of cases in neurology had MUS and the rate of misdiagnosis was less than 5%. In the field of neurology there was no information on disability, limited information on co-morbid anxiety and depressive disorders, and outcome studies were confined to conversion hysteria only. In the prospective cohort study 30% of new patients presenting to neurology out-patient clinics had MUS. They were as physically disabled by their symptoms as those with neurological disease were by theirs. They suffered from increased levels of pain and increased rates of anxiety and depression. At eight months follow up more than half the MUS patients were 'just the same' or 'worse'. There were no cases where unexpected neurological disease was diagnosed during the follow up which explained the patient's presenting symptoms. The patients with MUS had had multiple referrals to other specialist services as a result of MUS.
Conclusions- One third of new referrals to general neurology clinics have medically unexplained symptoms. These patients are disabled and distressed. Over half of these patients remain symptomatic at eight months follow up.

Declaration.

I declare that the contents of this thesis represent my own work unless otherwise stated.

Dr Alan J Carson MBChB, MPhil, MRCPsych.
15 October 2001

Contents

Chapter 1. Introduction.

Medically unexplained symptoms have been known by numerous synonyms over their long history. The first descriptions, four millennia ago, were of *disorders of the matrix* or *suffocation of the mother* (Merskey and Potter 1989). By the time of the Renaissance, the universal term was *hysteria* (King 1993), although some attribute this term to the classical era (Veith 1965). The Enlightenment saw the introduction of terms such as *functional disorder*s (Trimble 1982), subsequently modified to *functional somatic symptoms* (Wessley *et al* 1999). The twentieth century, under the influence of psychoanalysis, saw an explosion of terms: *psychoneuroses* (Freud and Breurer 1895), *conversion hysteria* (Freud and Breurer 1895), *conversion disorder* (APA 1984) and *somatization* (Steckl 1923). The effort to move from psychoanalytic theory to operationalised definitions brought more terms: *Briquet's syndrome* (Guze *et al* 1975), *somatization disorder* (APA 1984), *somatoform disorder* (Escobar *et al* 1987). Medical specialisation and sub-specialisation led to plethora of individual syndromes that could be included under the general heading of unexplained symptoms. The following list is far from exhaustive: *irritable bowel syndrome, fibromyalgia, chronic pelvic pain, non-cardiac chest pain, hyperventilation syndrome, chronic fatigue syndrome, tension headache, globus syndrome, multiple chemical sensitivity* (Wessley et al 1999).

This author prefers the term *medically unexplained symptoms* (MUS) for he agrees with Deary (1999) "that it is among the better descriptive terms because it brings honest

ignorance to the fore and states simply that there is a number of symptoms and syndromes that present as a phenomena for which health professionals at present can find no medical cause on the basis of physical examination or investigation."

In an examination of MUS the first question one must ask is: is this one disorder or many? Undoubtedly, the structure within which Western medicine is practiced has led to a tendency to separate the conditions covered by the general umbrella of MUS into a number of clinical entities as a result of the focus on the lead symptom and the body system in which it occurs (Wessley *et al* 1999). However, is the majority of the variance shared by the common term of MUS or by the individual clinical syndromes? On the basis of clinical presentations, Wessley *et al* (1999) mounted a persuasive argument that the similarities between individual syndromes outweigh the differences. In line with their hypothesis they demonstrated similarities in case definition, reported symptoms, and in non-symptom associations such as patients' sex, age, outlook and response to treatment. Deary (1999) used a different approach to the problem and utilised principal components analysis. He found that an unrotated principal component explained at least 40% of the total variance. In other words a sizable proportion of variance was explained by a predisposition to MUS in general. The addition of structural equation modeling helped to clarify the situation and suggested that there was a common predisposition to MUS, some coherent symptom groups which were highly correlated but nonetheless separable (such as somatic depression and chronic fatigue), and for each symptom group there was also a highly specific source of variance. Thus one can conclude that it

is legitimate to study MUS as a grouped variable for research when the purpose is general epidemiological information but for more fine grained aetiological studies and for the treatment of individual patients, specific symptom inquiries may also be beneficial. For the purposes of this thesis a general "lumping" approach has therefore been taken.

If one could, as noted, have justified studying MUS in any setting, or indeed a number of settings, why choose to study neurology patients? From an historical perspective one might find it hard to resist studying them. The study of MUS (or hysteria) has played a pivotal role in the development of both psychiatry and neurology. In psychiatry, the study of MUS has been intimately involved in the naming the discipline itself, moral treatment for the insane, the study of neuroses, the development of psychoanalysis, the backlash to operationalised criteria and the Diagnostic and Statistical Manuals of Disease. Neurologists will recognise the contribution the study of MUS has made to the development of clinical examination and in particular the study of reflexes, but also to specific diseases such as movement disorders and epilepsy. The study of MUS has also spilled over into philosophy and had a central role in conceptualising how we view the brain and its interaction with consciousness and a putative mind. Finally, in this author's opinion, the patients who present neurologically with medically unexplained symptoms comprise one of the most fascinating patient groups in medicine to study.

Epidemiological studies provide an indication of the scale of MUS as a problem. Patients with MUS account for 20-50% of primary care consultations worldwide, and exist in all cultures and across both sexes and all ages (Gureje *et al* 1997). Similar results have been found in secondary care settings, in general (Hamilton *et al* 1996), and in neurology specifically (Creed *et al* 1990).

Despite their high prevalence, surprisingly little is known about the consequences of MUS for patients. Although all doctors have a few highly disabled and time-consuming 'heartsink' patients on their lists, little is known about the degree of disability associated with MUS for the vast majority of patients who suffer them. Research on chronic fatigue syndrome (CFS; Komaroff *et al* 1996) has shown that far from representing the 'worried well' CSF is in fact associated with significant disability similar to other chronic 'organic' diseases.

The association between MUS and anxiety and depression (emotional disorders) has been long recognised (Burton 1676). The prevalence of these disorders in MUS patients is higher than in comparable medical patients (Walker *et al* 1997) There has been a recent research focus on the burden of disability caused by depressive illness, both in uncomplicated cases and in cases co-morbid with other physical diseases (Wells *et al* 1989, Frasure Smith *et al* 1995, Parikh *et al* 1990). One might hypothesise that depression will also contribute to the burden of disability in MUS patients.

Patients with severe somatisation disorder (Briquet's syndrome) have a poor outcome (Guze *et al*1986). This is not surprising given that chronicity is, in effect, a requirement for the diagnosis. However, much less is known about the outcome of MUS in general, and in neurological settings in particular. Potts and Bass (1995) found that three quarters of patients with unexplained chest pain were still symptomatic, and still unexplained, after 10 years follow-up. Nonetheless, some doubts do remain over the validity of the concept. The most outspoken critic has been Slater (1965) whose classic paper is still viewed by many as a warning. He claimed that almost two thirds of those diagnosed with hysteria in fact had organic neurological disease. A repeat of the study (Crimlisk *et al* 1998), in the same setting, but with superior methodology, repudiated Slater's claim. However, there can be little doubt that it is Slater's study that remains influential.

Another concern of many doctors, and health service managers, is the resources MUS patients may utilise. Some indite this concern. Why should MUS patients be the only group in which the primary outcome measure for treatment studies is cost not efficacy (Kroenke 1999)? Again, the evidence of resource use comes mainly from studies of severe somatisers (Fink 1992) and much less is known of the behaviour of the majority of patients with MUS.

If emotional disorders do contribute to the burden of disability in MUS patients, there is little prognostic data to aid prediction of what their effect might be over time. What evidence exists (Mayou and Hawton 1986), suggests that many of the emotional disorders diagnosed in general medical patients spontaneously remitted after contact with the hospital had ceased. However, there has been some recent evidence suggesting that such emotional disorders persisted and influenced the outcome of myocardial infarction (Frasure-Smith *et al* 1995) and stroke over periods of two year follow-up (Parikh *et al* 1990).

Sydenham, the great English physician, considered that managing patients with MUS represented a true test of a doctor's skill and sagacity (Sydenham; trans Latham 1848). More recently, it has been recognised that patients with severe MUS are indeed a "heartsink" (incidentally, a phrase used by Sydenham to describe the patient's, not the doctor's, emotions) and they are perceived as difficult to help (Walker 1997). It is also frequently said that those with MUS are unwilling to seek psychiatric/psychological help. Such statements certainly apply to those at the severe end of the spectrum but whether they apply to the majority of patients with MUS is more open to question. The evidence appears to be anecdotal on the basis of extrapolation from severe cases and formal studies are lacking.

This thesis is addressed at these issues. It is comprised of three parts. In the first part, the methods used in the thesis will be described. This will begin with a description of the specific aims of individual chapters, then a description of the methods used to achieve these aims. The closing chapter, in this section, will explain the rational and justification behind the choice of the main measures used in the original research part of the thesis. The discussion in this chapter will be in greater detail than that given in a standard methods description and is therefore presented separately as an aid to comprehension.

The middle section of the thesis consists of a literature review on medically unexplained symptoms. This commences with an historical review of the topic from the very first medical texts (2000 BC) to the middle of the twentieth century. The next chapter provides a narrative overview of the field of medically unexplained symptoms in order to provide a context within which the specific findings on MUS in neurology can be viewed. The final chapter of the literature review consists of a systematic review of the literature on MUS in neurology since 1960.

The final part of the thesis describes the results of a prospective cohort study of 300 new referrals to neurology clinics. The patients were examined at initial assessment for MUS, disability and distress. Their outcome was measure at eight months follow up in terms of clinical global improvement, diagnostic validity, disability, distress and service utilisation.

Chapter 2. Aims

Chapters 3 and 4 will outline and justify the methods of study used in this thesis. The aims of the remaining chapters are described below.

Chapter 5. Medically unexplained symptoms: an historical review.

To describe the way in which clinical signs and descriptions of medically unexplained symptoms have interacted in successive historical periods, with reference to their scientific, psychological, political, social and cultural context.

Chapter 6. Medically unexplained symptoms: a narrative review.

To describe the currently available body of knowledge on non-neurological medically unexplained symptoms, with particular emphasis on frequently cited studies that are either of potential interest to this thesis or influential on current concepts and practice.

Chapter 7. Medically unexplained symptoms in neurology: a systematic review.

To systematically ascertain and evaluate all relevant studies on medically unexplained symptoms in neurology to estimate prevalence, diagnostic stability, associated disability and distress, outcome, and health care utilisation.

Chapters 8-13. Medically unexplained symptoms in neurology: a prospective cohort study of 300 consecutive new referrals to general neurology out-patient clinics.

Chapter 8. Do medically unexplained symptoms matter?

To determine the proportion of patients newly referred to general neurology outpatient clinics who have medically unexplained symptoms and their associated levels of disability and distress.

Chapter 9. Depression anxiety and health status; are they related?

To determine the prevalence of anxiety and depressive (emotional) disorders among new attenders at general neurology outpatient clinics and whether emotional disorders contributed to disability and health status in MUS patients.

Chapter 10. What is the outcome of medically unexplained symptoms in neurology?

To determine the outcome of neurological out-patients with medically unexplained symptoms at eight months follow up.

Chapter 11. What is the outcome of depressive disorders in neurology?

To determine the outcome of depressive disorders in neurology out-patients eight months after the initial diagnosis and to examine whether a change in depression status (depressed to not depressed, or not depressed to depressed) was associated with a change in overall health status.

Chapter 12. What health care resources have patients identified with medically unexplained symptoms in neurology used?

To estimate the lifetime use of health care resources by neurological out-patients with medically unexplained symptoms.

Chapter 13. How were patients with medically unexplained symptoms perceived?

To determine whether neurologists found patients with medically unexplained symptoms more difficult to help.

Chapter 3. Methodology

The methods used in individual chapters are described below.

Chapter 5. Medically unexplained symptoms: an historical review.

The fundamental methodological issue in addressing a history of medically unexplained symptoms is deciding upon the unit of study (Micale 1990). Should it be the scientific researcher, the medical theory, the practising clinician, the suffering individual, the hospital, or the professional collectivity? For the purpose of this review, a modified version of the definition used by Berrios and Porter will be used.

"The history of clinical psychiatry may be defined as the study of the way in which clinical signs and their descriptions have interacted in successive historical periods, and of their psychosocial context." (Berrios and Porter 1995).

This review will aim to *describe* rather than to *study*. Two particular areas of methodological difficulty were noted. First, Micale (1990) has warned that 'in-house' histories are prone to the danger of being used as sources of prestige to the profession rather than as critical evaluations. He, along with Berrios and Porter (1995) suggest that studying medical history is the work of historians. Whilst, this undoubtedly true in terms of technique, and the ability to access and critically assess primary source material, it should be remembered that this too has its flaws. Most importantly, psychoanalytic theory and its use as a major critical tool has dominated arts education in

Western universities in the post-war era (Findlay 1995). Thus, historians have an inevitable bias in the way they approach psychiatry, the specialty from which psychoanalysis grew. Even Porter (1997), considered by Micale (1990) to be truly impartial, finishes his brief history of psychiatry on a note of warning:

"The trump card of a new science of the brain has often enough been played, unsuccessfully, in the history of the discipline, and the claims of brain scientists to understand consciousness and its terrors have been shown to be shallow, indeed deluded." (Porter 1997)

Second, semantics are a particular source of potential bias in both clinician and historian based historiographies. For example, clinicians frequently refer to Hippocrates' description of melancholia unaware that it was then a term for insanity in general rather than its current meaning of a severe major depressive disorder with marked somatic features (Berrios 1988). Equally the reverse occurs and historians overanalyse the semantic derivation of terms and miss their clinical importance. King (1993), for instance, makes an impressive semantic argument that the actual term *hysteria* never appeared in classical times, but from the clinical perspective this is almost totally irrelevant as, even she acknowledges, a wide range of (hysteria-like) symptoms were described and attributed to a uterine causation.

Owing to both the potential methodological problems and also economies of time, this review did not aim to discover new source material or reanalyse the historiography of medically unexplained symptoms. Rather, it aimed to assimilate and describe currently existing ideas in line with Berrios and Porter's definition.

There were two main sources of material. First, four textbooks of medical history were consulted:

i. Zilboorg's (1941) *A history of Medical Psychology*, described as a 'whig' history of psychiatry (Micale 1990).
ii. Veith's (1965) standard text *Hysteria. A history of a disease*, which offered an historiography from the perspective that Freud's theories were 'final'.
iii. Porter's (1997) *The greatest benefit to mankind. A medical history of humanity from antiquity to the present,* a modern social history of medicine.
iv. Berrios and Porters (1995) *A history of clinical psychiatry. The origins and history of psychiatric disorders*, which represented an attempt to marry clinical and social histories.

These texts were used to provide an intellectual and social structure to the four millennia which the review covers. They acted as sign posts to the important texts and documents on the topic through history.

Second, individual references were consulted, read and interpreted in light of the texts above, but also influenced by the author's own clinical experience and understanding of the area. These were supplemented by other texts and papers the author was aware of, or that were taken from reference lists from papers retrieved by the method described above. As the aim was to describe, rather than interpret, direct quotation was frequently used to demonstrate the ideas of key theorists.

The historical approach was terminated with Elliot Slater's (1965) paper. This point in time was chosen to switch the method of review to an evidence based medicine approach (Sackett et al 1997). This was because Slater's paper remains the single most influential work in the area and it was therefore appropriate to judge it, not just in the context of its own time, but also in light of modern epidemiological standards as it is still influencing a current practice.

Chapter 6. Medically unexplained symptoms in neurology: a narrative review

This section of the literature review was a traditional narrative review of other relevant papers on MUS. The chapter reviews epidemiological studies, the effects of depression on physical symptoms, aetiological theories and treatment. There were no specific entry criteria for papers, and eligibility was at the discretion of the author. The inherent biases in this process were acknowledged (Oxman and Guyatt 1993). Unfortunately, a systematic approach to paper selection would be beyond the scope of this thesis.

Chapter 7. Medically unexplained symptoms: a narrative review.

All studies, but not case reports, from 1960 to 31st January 2000 that described medically unexplained symptoms in patients attending either neurology in, day or out-patient units were potentially eligible for inclusion. In addition they had to describe data potentially relevant to the aims of the subsections listed below.

i. What is the prevalence of MUS in neurology clinics?
ii. How valid is the diagnosis of MUS in neurology patients?
iii. What is the association between MUS and health status in neurology patients?
iv. Are MUS associated with anxiety or depressive disorders?
v. What is the outcome of MUS in neurology patients?
vi. What other health services do neurological patients with MUS use?
vii. Do neurologists find patients with medically unexplained symptoms difficult to help?

The search strategy used is shown in Table 3.1. All on-line abstracts were reviewed and only rejected if clearly ineligible. This search was supplemented by papers known to the author and by papers from the reference lists of papers retrieved by the search strategy.

All studies were reviewed in accordance with Sackett *et al*'s (1997) recommendations. The following questions were asked of all included studies:

1. Was there a clearly defined sample of patients?
2. Was there a comparison group similar in all other important ways except the presence of MUS?
3. Was the sample representative?
4. Were objective initial assessment criteria applied?
5. Were initial assessment criteria applied blind?
6. Was the follow-up of patients complete (>70%)?
7. Were objective outcome criteria applied?
8. Were outcome criteria applied blind?

In order to allow the easy assimilation of information a numerical quality score was calculated for each study by the simple addition of one point for each of the above criteria that were satisfied. Such a strategy is properly used for the analysis of randomised controlled trials (Moher 1998) where the effects of biases are more predictable. The assessment of quality was therefore supplemented by an exploration of potential sources of bias as recommended for systematic review of observational studies (Egger 1998).

Table 3.1. **Search strategy for systematic review of medically unexplained symptoms in neurology.**

	Search History	Result
1	Hysteria	2 362
2	Explode psychophysiologic disorders	14 041
3	Explode somatoform disorders	6 475
4	Explode conversion disorder	1 227
5	Explode factitious disorder	1 609
6	Explode dissociative disorder	1 531
7	Hysteria. textword	2 188
8	((dissoc$ or psychosomatic or physiological or psychogeneic or somati$ or unexplained or conversion)adj5(disorder or symptoms or illness))	157 091
9	(disorder or symptoms or illness).textword	309 146
10	Somati#ation.textword	1 315
11	Non-organic.textword	344
12	((dissoc$ or psychosomatic or or conversion or psychophysiological or psychogeneic or somati$ or unexplained)adj5(disorder or symptoms or illness)).textword	4 862
13	1 or 2 or 3 or 4 or 5 or 6 or7 or 10 or 11 or 12	27 789
14	Explode paralysis	45 592
15	Explode psychomotor disorders	2 791
16	Paresis	985
17	Explode movement disorders	30 990
18	Par?esthesia	2 832
19	Hypesthesia	924
20	Hyperesthesia	465
21	Explode dominance, cerebral	29 553
22	Explode neuromuscular disease	37 428
23	Explode disabled persons	15 883
24	Laterality .textword	2 134
25	(motor or paralysis or paresis or hemiparesis or paraparesis or tetraparesis or weakness or par?esthesia or hypesthesia or hyperesthesia or wheelchair).textword	112 415
26	(sens$ adj (symptom$ or disturbance or complaint)).textword	1 049
27	14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or	243 867
28	13 or 27	1 328
29	(21 or 24) and 25 or 26 or hyperventilation)	3 233
30	Conversion disorder	1 227
31	28 or 29 or 30	5 589

Chapters 8-13. Medically unexplained symptoms in neurology: a prospective cohort study of 300 new referrals to neurology out-patient clinics:

Setting:

The study was conducted in the out-patient clinics of a regional neurology service for Edinburgh and Lothian, Scotland. The clinics were conducted by eight consultants and their junior staff. All the outpatient clinics accepted general referrals, which were allocated by clerical staff according to available appointments. Clinic templates dictated the number of urgent, semi urgent and routine appointments available in each clinic. The case mix was very similar to that described for other services (Perkins 1989). Specialised clinics also existed for memory disorders, neurovascular disorders and epilepsy.

Sampling:

The study was conducted between November 1997 and March 1998 in five of the eight consultant outpatient clinics (CW, RG, CL, CM, AZ see acknowledgements). Some patients were seen initially by a specialist registrar, but their cases were reviewed by a consultant at the time of initial consultation. Limiting the number of clinics to five allowed one clinic to be studied each weekday. All new patients were included except in one clinic where, because of the large number attending, every alternate new patient was included.

Initial assessment, procedures and measures:

The ratings of the degree to which the patients' symptoms were considered to be 'medically explained' were obtained from the consulting neurologist. They rated their opinion on a four point Likert scale immediately after the initial consultation:

To what extent can this patient's symptoms be explained by organic disease?

Not at all *Somewhat* *Largely* *Completely*

This was referred to as the 'organicity rating'. Such a system has been shown to be reliable and valid (Speckens 1996, Crimlisk 1998).

In order to determine the validity of these ratings for this sample the neurological case notes were reviewed six months later (by AC or JS), after further assessment and investigations had been performed. The treating neurologist was consulted if clarification was necessary. The final diagnosis was recorded and any change in opinion regarding the 'organicity' of the complaint noted.

Prior to their patient's attendance at the clinic, the general practitioner (GP) was sent a brief questionnaire asking them to indicate why they had referred the patient by endorsing one of four reasons listed.

What was your main reason for referring (patient name) to the neurology out- patient clinic?

i. *Patient needed neurological diagnosis and possible treatment*

ii. *Patient requested referral*

iii. *To reinforce my opinion that there was no neurological disease*

iv. *Other*

New patients were sent details of the study in advance of their attendance at the clinic. Following their consultation with the neurologist, patients were approached by the researchers and informed consent for participation sought. Those who agreed to participate were assessed (by AC or BR) using a combination of structured interviews and self rating questionnaires, within seven days of their neurological consultation.

Patients' perceptions of health status and disability were measured using the Medical Outcome Study Scale (SF-36; Ware et al 1982). This self-report scale examined health status in eight domains: general health perceptions, physical functioning, physical role functioning, bodily pain, social functioning, vitality, mental health and emotional role functioning. It was scored as recommended by its authors (Medical Outcomes Trust 1994). In all domains of the SF-36 scores range from 0 to 100. A lower score was indicative of poorer health status (ie worse functioning or increased pain).

Patients also completed a checklist that inquired about the fifteen most common somatic symptoms, excluding upper respiratory tract infections, with which patients present to

primary care physicians (Schappert 1989, Kroenke et al 1990; table 3.2). This was to obtain a measure the number of different physical symptoms they suffered.

The presence of anxiety and depression disorders (emotional disorders) was measured using a combination of a self-report scale and a structured interview. Patients completed the self-rated Hospital Anxiety and Depression Scale (HAD; Zigmond and Snaith1983) designed for use with patients who have co-morbid medical conditions. Psychiatric diagnoses, according to the DSM IV classification (APA 1994), were made using the Primary Care Evaluation of Mental Disorders (PRIME-MD; Spitzer et al 1994). This is a brief structured interview of proven reliability and validity. Although subjects were asked to complete the PRIME MD questionnaire it was not used as a screening instrument and all subjects completed the diagnostic interview in full. The specific diagnoses included in the category 'emotional disorder' were major depression, minor depression (research criteria, Appendix B, DSM IV), dysthymia, panic disorder, generalized anxiety disorder and anxiety disorder not otherwise specified.

A specific enquiry about suicidal ideation was conducted as part of the PRIME MD schedule. All patients were asked:

"In the last two weeks, have you had thoughts that you would be better off dead or of hurting yourself in some way?"

Table 3.2. **Rating scale for the number of physical symptoms suffered by the subject.**

During the PAST MONTH have you been bothered A LOT by:

	YES	NO
Stomach pain	[ ]	[ ]
Back pain	[ ]	[ ]
Pain in your arms, legs or joints (knees, hips, etc)	[ ]	[ ]
Menstrual pain or problems	[ ]	[ ]
Pain or problems during sexual intercourse	[ ]	[ ]
Headaches	[ ]	[ ]
Chest pain	[ ]	[ ]
Dizziness	[ ]	[ ]
Fainting spells	[ ]	[ ]
Feeling your heart pound or race	[ ]	[ ]
Shortness of breath	[ ]	[ ]
Constipation, loose bowels or diarrhoea	[ ]	[ ]
Nausea, gas, or indigestion	[ ]	[ ]
Feeling tired or having low energy	[ ]	[ ]
Trouble sleeping	[ ]	[ ]

If they answered yes, they were asked to go on to describe to the interviewer the nature of these thoughts. To be classed as having 'suicidal ideation', the patient had to have considered *active plans* (such as buying paracetemol in order to take an overdose) for committing suicide nearly every day for the previous two weeks. Whenever a patient reported such ideation the general practitioner was informed.

Assessments were carried out by AC or BR both of whom had been trained in the use of the assessment instruments. At the time of assessment researchers were blind to the neurologists' and general practitioners' assessments. A sample of 50 of BR's interviews were tape recorded and re-rated blind by AC to check reliability. Only one case was categorised as having a psychiatric disorder by BR when in the opinion of AC they failed to meet criteria.

Follow-up assessment:

A follow-up assessment was conducted on all participating patients eight months after their initial assessment. Interviews were conducted by telephone. When a subject had no telephone, or preferred to see the interviewer, or where there was communication difficulty a face-to-face interview was conducted. There is good agreement between telephone and face-to-face diagnostic interviews (Wells 1988). Patients completed a five point Clinical Global Improvement scale (CGI; Guy 1976) as well as repeating the measures used in the initial assessment. The interviews were conducted by AC and KP both of whom had been trained in the use of the assessment tools.

An additional investigation was conducted on all patients who were diagnosed as having medically unexplained symptoms at initial assessment. Their primary care case records were examined and their case was discussed with their general practitioner (by AC or SB). The following were recorded: any change in diagnostic opinion, on-going treatments, the number of primary care contacts per annum, and any referrals to other medical disciplines and the outcome of that referral. An estimate was made as to whether other specialist referrals had been due to MUS or 'organic disease. Symptoms were only classed as MUS if this was explicitly stated by the specialist or if the diagnosis was made of a typical MUS syndrome (eg fibromyalgia, irritable bowel syndrome, chronic fatigue). If there was any doubt about the opinion or the outcome the symptom was classed as 'organic'.

How patients with medically unexplained symptoms were perceived:

Following the initial consultation neurologists were asked to indicate how difficult they found the patient to help on a four point Likert scale (Sharpe et al 1994):

To what extent do you find this patient to help with the problems they present?

Not at all difficult *Somewhat difficult* *Very difficult* *Extremely difficult*

Patients' perception of need for any form of psychiatric/psychological treatment was recorded by a simple yes/no checklist before and after their consultation. GPs made a

similar rating prior to the patients attending the neurologists. The neurologists made their rating following the consultation.

Statistical Analyses:

The strategies used for analysing data to answer the individual aims are described immediately prior to the relevant results sections.

Ethical approval:

The study was approved by the local research ethics committee. All participants gave informed consent for participation.

Chapter 4. Justification of measures.

4.1 Introduction.

This brief chapter aims to justify the selection of the main measures used in the study. It outlines the rational behind the choice of measures used and details the available data on reliability and validity.

4.2 The 'organicity' rating:

The rating of whether or not a patient has medically unexplained symptoms is central to the study and it must be decided *a priori* what is to be measured and categorised as MUS. The literature reviews demonstrated that MUS could be regarded as literally any symptoms which lack both a medical diagnosis and some underlying pathology in the traditional sense of the bio-medical model. Alternatively at the other extreme there is the rigid definition of somatization disorder in DSM IV (APA 1994), which offers a highly restricted concept similar to Briquet's syndrome (Guze 1975). There is no doubt that this later definition is a well-validated construct and thus potentially the definition of choice. However, it defines the extreme end of the spectrum and the majority of patients presenting at out-patient clinics with putative MUS will not meet the high symptom threshold (Katon *et al* 1991, Kirmayer and Robbins 1991). Furthermore it necessitates a detailed enquiry about lifetime symptom experiences which are typically not feasible in medical out-patient clinics (Simon and Gureje 1999). Therefore, whilst it may be reliable and valid (Perley and Guze 1962) it does not have much practical

utility. In recognition of this problem Spitzer *et al* (1994) proposed multi-somatoform disorder which they defined as 3 or more unexplained symptoms plus a two year history of somatization. They have demonstrated the stability of the concept over time (Kroenke *et al* 1997). This definition defines the symptoms of around 30% of those who attend out-patient clinics with putative MUS, but does not help with description of the other 70%. A similar approach has been taken by Escobar *et al* (1983) using the somatization disorder probes from the Diagnostic Interview Schedule (Robins *et al* 1981) but lowering the proposed cutoff.

Yet, the working clinician needs to be able to offer diagnosis and prognosis on all those who attend his or her clinic and will also recognise that not all patients fit neatly into diagnostic categories. In response to this researchers have tried for more flexible, but potentially more clinically meaningful definitions of MUS. It is recognised that such definitions may be less robust.

One commonly used method has been retrospective case note evaluation of whether or not individual symptoms were or were not 'organically' explained. Whilst this has been a common methodology in studies cited in this thesis, it has several flaws. First, none of the cited studies offer any operationalised criteria for what was judged to be medically unexplained. Second, none of the studies had any system to check observer reliability. Third, this system is overly reliant on laboratory investigations to indicate abnormalities, particularly as case notes can be written in "code" for such patients,

perhaps through fear of causing offence should the patient request access or perhaps through fear of litigation. The method is also prone to the selection biases of retrospectively defined cohorts (Lewis and Mann 1992).

An alternative technique that rated 'organicity' of symptoms on a visual analogue scale (VAS) was proposed by Metcalfe *et al* (1988) and repeated by Ewald *et al* (1994). Neurologists scored 'organicity' on a 10cm visual analogue scale. The technique has been shown to be reliable (intra-rater) within the context of a single admission (*Creed et al* 1990). The problem is with interpretation. Metcalfe proposed that all scores within 10mm of the organic end of the VAS be classed as neurological disease and all those within 10mm of the opposite end as non-organic. All scores on the middle 80mm were labeled as in between. Where the cutoff is drawn is of obvious importance. The 10mm cut-off, as opposed to 20mm or 30mm, as a measure of neurologists' opinion that a symptom was medically unexplained has not been tested against any other standard. Thus using this technique to make comparisons of degree of 'organicity' of symptoms between two or more groups may be valid, but using it to define the number of patients with MUS is flawed.

A preferable approach was offered by Speckens *et al* (1996) and Crimlisk *et al* (1998) who utilised Likert scales. These scales are the most widely used and the most useful of a summated rating scales (Peck 1993). They offer the advantage of defining cutoffs more accurately. The technique has greater content validity and is more easily testable

for inter-rater and predictive validity and it does perform satisfactorily in the above studies. However, the Speckens *et al* study, although prospective in design, only offered three intervals on their scale. It is generally considered desirable to avoid a neutral step as they often introduce response bias (Kugler 1992). The Crimlisk *et al* study, although weaker as it was retrospective, offered a four-point scale. A variation of this was therefore used in this study.

4.3 The assessment of health status and disability:

It is now generally accepted that patient's point of view should be regarded as central in monitoring medical outcomes (Geigle and Jones 1990). However, the core problem is that there is no clear, universally accepted definition of 'health' or quality of life and what its constructs should be (Spikler1996). The World Health Organisation conceptualises health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity". Whilst commendable this definition clearly lies outside the scope of most traditional medical specialties with such issues as opportunity, education and social security being regarded as the responsibilities of government not individual medical practitioners. Schipper *et al* (1996) offered an alternative definition using the construct of 'Quality of Life' which they define "...in clinical medicine represents the functional effect of an illness and its consequent therapy upon a patient as perceived by the patient". They regard this definition as being made on the premise that "the goal of medicine is to make the morbidity and mortality

of a particular disease disappear. What we seek to do is to take away the disease and its consequences and leave the patient thereafter as if untouched by the illness."

Over the last 20 years a number of new scales (Amercian Cancer Society 1984, Wenger *et al* 1984, Lohr and Ware 1987, Lohr 1989) have been tested for reliability and validity in the search for a scale that will allow measurement of general health status without being specific to any age, sex, disease or treatment groups. As with all scales there is both a trade-off between breadth and depth and also between information gained and time needed for administration. The Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) was designed specifically to bridge the gap between thorough but lengthy health surveys aimed for specific research projects (Brook *et al* 1979) and the relatively coarse single item health measures used in national surveys (Spitzer *et al* 1981). It aimed to provide a comprehensive, psychometrically sound, yet brief, standardised health survey (Ware and Sherbourne 1992). Of most importance to the SF-36 is its construct validity, the accumulation of evidence of validity in relation to theoretical constructs. The assessment of this requires three steps (Nunnally 1978): (1) specifying the domain of the variables; (2) establishing the internal structure of the observed variables and; (3) verifying theoretical relationships between scale scores and external criteria.

In examining the first step, the rationale behind the domains studied has been clearly described (Ware and Sherbourne 1992). In essence it was a consensus opinion and they

examined the domains that they and others had found to hold most face validity when discussing a multi-dimensional approach to health status. This led to the studying of 40 items in the Medical Outcomes Study from which eight were selected; physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health (Stewart and Ware 1992). The items selected represented those most commonly used in other health surveys and those most affected by disease and treatment (Ware 1993, Ware *et al* 1995). Among the potentially important omissions were spiritual, sexual and intellectual domains (Ware 1996).

The results of examination of internal structure (step 2) are shown in table 4.1. The eight scales used can be factor analysed into Physical Health Component Summary (PCS) and Mental Health Component Summary (MCS) measures which account for 80% to 85% of the variance (Ware et al 1994). Three scales (physical function, role physical and bodily pain) correlate most highly with the PCS and contribute to most of the score. By comparison two variables (role emotional and mental health) contribute most exclusively to the score of the MCS. Three variables (social function, vitality and general health) contribute to both summary measures. Of most interest mental health score was the poorest predictor of physical function score and vice versa.

In tests against external criteria (step 3) the SF-36 has been validated against accepted clinical indicators in heart disease, diabetes mellitus, depression and several other

Table 4.1. **Summary of information about SF-36 scales and physical and mental component summary measures (Ware *et al* 1994).**

	Correlations		Number of					
Scales	PCS	MCS	Items	Levels	Mean	SD	Reliability	95% C.I.
physical functioning	0.85	0.12	10	21	84.2	23.3	0.93	12.3
role-physical	0.81	0.27	4	5	80.9	34.0	0.89	22.6
bodily pain	0.76	0.28	2	11	75.2	23.7	0.90	15.0
general health	0.69	0.37	5	21	71.9	20.3	0.81	17.6
vitality	0.47	0.65	4	21	60.9	20.9	0.86	15.6
social functioning	0.42	0.67	2	9	83.3	22.7	0.68	25.7
role-emotional	0.16	0.78	3	4	81.3	33.0	0.82	28.0
mental health	0.17	0.87	5	26	74.7	18.1	0.84	14.0
physical component summary (PCS)			35	567	50.0	10.0	0.92	5.7
mental component summary (MCS)			35	493	50.0	10.0	0.88	6.3

conditions (Ware *et al* 1995). The interpretation of scores on the SF-36 is described in table 4.2.

Reliability tests of the eight subscales and two summary estimates using both test-retest and internal consistency methods have almost always exceeded 0.80 for the subscales and 0.90 for the summary estimates (Ware *et al* 1993, McHorney 1994).

Whilst the SF-36 scale has its flaws and its critics, predominantly on grounds of its scope and the potential for floor and ceiling effects, it is undoubtedly the most widely used measure of health status. This offers considerable advantages as a research tool. Its reliability and validity have been tested in numerous patient and community-based samples as well as geographical locations. In particular, it has been tested within Lothian and was found to be reliable and valid (Cohen *et al* 1994). Its reliability and validity when used in telephone interviews has also been well described (Ware *et al* 1993).

Although the validity of the SF-36 has been extensively tested as described, it is important to note that some of this testing has been specifically in groups with mental disorder, rather than measuring mental distress in the normal population. The MOS scale and the SF-20 have been shown to be reliable and valid measure of health status and disability in patients suffering form mental disorder (Wells *et al* 1989, Spitzer *et al* 1995). The Spitzer *et al* study looked at health status across different groups of mental

Table 4.2. **Interpretation of SF-36 sub scale scores (Ware *et al* 1995).**

	Definitions (% observed)	
Scales	Lowest possible score	Highest possible score
Physical functioning	Very limited in performing all physical activities including bathing and dressing (0.8%)	Performs all types of physical activities including the most vigorous without limitations due to health (38.8%)
Role-physical	Problems with work or other daily activities as a result of physical health (10.3%)	No problems with work or other daily activities (70.9%)
Bodily pain	Very severe and extremely limiting pain (0.6%)	No pain or limitations due to pain (31.9%)
General health	Evaluates personal health as poor and believes it is likely to get worse (0.0%)	Evaluates personal health as excellent (7.4%)
Vitality	Feels tired and worn out all the time (0.5%)	Feels full of pep and energy all the time (1.5%)
Social functioning	Extreme and frequent interference with normal social activities due to physical and emotional problems (0.6%)	Performs normal social activities without interference due to physical or emotional problems (52.3%)
Role-emotional	Problems with work or other daily activities as a result of emotional problems (9.6%)	No problems with work or other daily activities (71.0%)
Mental health	Feelings of nervousness and depression all of the time (0.0%)	Feels peaceful, happy and calm all of the time (0.2%)

disorder and found differing patterns of impairment. They argue that this makes unlikely that patients with mental disorders simply exaggerate the actual amount of their disability.

4.4 The diagnosis of anxiety and depressive disorders:

The five phases necessary for establishing diagnostic validity in psychiatric disorders have been described by Robins and Guze (1970). They consisted of clinical description, laboratory studies, delimitation from other diagnoses, follow-up and family studies. Following this move, the utilisation of structured interviews and operationalised diagnostic schemata have provided vehicles for the systematic progress in the refinement and validation of diagnoses (Rice *et al* 1992). It has therefore become necessary to validate both the diagnostic instrument as well as the underlying construct. A complete discussion of the process of validation of the construct of depression as a diagnosis is beyond the scope of this section, but has been well described by Kendell (1975), Rice *et al* (1992) and Jablensky (1988). It shall be assumed that depression, as defined in DSM IV, is a valid construct, and the remainder of the section will concentrate on the reliability and validity of the diagnostic instruments used in this thesis.

The literature reviews indicate that the psychiatric diagnoses most commonly made in neurology out-patients are major depressive disorder, minor depressive disorder, dysthmia and anxiety disorders. By contrast, bipolar disorder and schizophrenia are

relatively rare. It was therefore desirable to use a interview tool that targeted these symptom areas. Clinical experience also dictated that making psychiatric diagnoses in 'medical' patients can be a sensitive area and that it is preferable to avoid interview schedules that concentrate on hallucinatory or delusionary experiences. A further consideration was to use a schedule that was easy to administer so that disruption to subjects would be minimal.

Two diagnostic interview schedules were potentially relevant: The Clinical Interview Schedule (CIS; Goldberg *et al* 1970) and the Primary Care Evaluation of Mental Disorders (PRIME MD; Spitzer *et al* 1994). The latter schedule had the advantage of diagnosing specific mental disorders according to DSM IV criteria, whereas the former provided an index of 'caseness'.

The PRIME-MD was developed from the Structured Clinical Interview for DSM III-R (SCID) which is a diagnostic interview schedule of proven reliability and validity (Spitzer *et al* 1992). The PRIME-MD's sensitivity and specificity was examined against the SCID in the PRIME-MD 1000 study (Spitzer *et al* 1994). In this study mental health professionals (MHP; either PhD psychologists or senior psychiatric social workers) who had been trained in the use of the SCID conducted blind interviews on 431 of a possible 536 patients who had been interviewed by Primary Care Physicians using the PRIME-MD. Participating subjects also completed self report measures of depression (Zung Depression Scale; Zung 1965) and anxiety (Zung Anxiety Scale; Zung 1971). The

results are shown in table 4.3. It can be seen that diagnoses were specific, however there were some problems with sensitivity.

To allow comparison with established patient self rating scales partial correlation coefficients were calculated against Zung Depression and Anxiety Scales. The partial correlation between any PRIME-MD mood disorder and scores on the Zung Depression Scale was 0.58 ($p<0.001$). The partial correlation for any PRIME-MD anxiety disorder and scores on the Zung Anxiety Scale was 0.53 ($P<0.001$).

The accurate diagnosis of major depressive disorder (as it was the emotional disorder most likely to be associated with poorer health status) was the main concern. Therefore, the PRIME-MD was considered adequate for the purposes needed. Furthermore, the problem with sensitivity appeared to be due to use of a one-page patient screening questionnaire. Only patients who responded positively to the screening probes were interviewed with the relevant sections of the interview schedule. An attempt was therefore to improve the sensitivity by conducting the full interview on all subjects, irrespective of responses to the screening questionnaire.

Table 4.2. **Indexes of agreement between PRIME-MD diagnoses made by primary care physicians using the PRIME-MD and Mental Health Professionals using the SCID (n=431; Spitzer *et al* 1994).**

	Sensitivity,%	Specificity,%	Positive Predicitive Value, %	Overall Accuracy Rate, %	κ
Any psychiatric diagnosis	83	88	80	86	0.71
Any mood disorder	67	92	78	84	0.61
Major depressive disorder	57	98	80	92	0.61
Partial remission of MDD	26	96	41	89	0.26
Dysthymia	51	96	56	92	0.49
Minor depressive disorder	22	94	19	89	0.15
Any anxiety disorder	69	90	60	86	0.55
Panic disorder	57	99	68	96	0.60
Generalised anxiety disorder	57	97	55	94	0.52
Anxiety disorder NOS	33	91	31	84	0.23

Chapter 5. Medically unexplained symptoms: an historical review.

5.1 Introduction.

This chapter will aim to describe the way in which clinical signs and descriptions of medically unexplained symptoms have interacted in successive historical periods, with reference to their scientific, psychological, political, social and cultural context.

The chapter will begin with the earliest known medical texts (2000BC) and continue chronologically to the current day. It should be recognised by the reader that what was labelled as *hysteria* or *disorders of the matrix* in the Classical era was certainly a much broader concept than the one of modern conversion disorder. It is undoubtedly the case that much of what was described under the rubric of hysteria had a pathological mechanism unrelated to either MUS or uterine conditions. However, there is a clear intellectual link between these clinical descriptions and the clinical descriptions of hysteria in the sixteenth and seventeenth century, which in turn can be seen to have a distinct overlap with the modern concept of MUS. Indeed DSM IV somatization disorder is heavily based upon Paul Briquet's description of hysteria. It was only following the twentieth century and the rise of psychoanalysis that hysteria became synonymous with the idea of psychic conversion. The meaning of hysteria will thus change as the chapter moves through the ages but it is hoped that reader will be able to follow the changes.

5.2 Disorders of the matrix in the ancient world.

Hysteria rivals epilepsy as the oldest disease known to medicine (Trillat 1995). It was the subject of the earliest existing medical text, dating from 1900BC, the *Kahun Papyrus* (Veith 1965). The papyrus was discovered in the ruins of the ancient Egyptian city whose name it bears. Unfortunately, only fragments remain, describing a series of morbid states attributed to either 'starvation' of the uterus or its upward displacement leading to crowding of other organs. The cases described include "a woman who loves bed; she does not rise and does not shake it" and "a woman aching in all her limbs with pain in the sockets of her eyes" (Griffith 1898).

This interpretation of the Kahun papyrus was not without controversy. It was argued by King (1995) that an Egyptian description of hysteria simply did not exist and the disorder had its origin during the Renaissance. King mainly draws her arguments from the work of Merskey and Potter (1989) which re-examined the content of the Kahun papyrus. They contest the view that the papyrus states explicitly that the uterus moved. They claim that the original translator of the papyrus, Griffith, mistranslated this section of the document. Their view is supported by the terse writing style used in the papyrus which gave 34 prescriptions for gynaecological disorders in approximately 3 pages. It was intensely practical in nature with no room for aetiological theories. Nonetheless, Merksey and Potter acknowledge that disorders of the eyes, neck, mouth, limbs, and urine were all described and attributed to a uterine causation, even if the mechanism was unclear.

Why the uterus came to be associated with the range of phenomena typical of MUS is unknown. However, whether it moved or lay still, a uterine theory was completely accepted and no other aetiological causes were discussed (Veith 1965). This suggests a strong tradition, perhaps oral, predating the Kahun papyrus. Veith hypothesises that observation of patients with uterine prolapse may have been of significance. One might also hypothesise that the normal changes during pregnancy may have been responsible for the link. Many of the conditions associated with MUS: heartburn, gastric reflux, altered bowel habit, lethargy, muscular aches and pains are part of the routine experience of pregnancy, and are indeed caused by upward pressure of the uterus on other visceral organs.

Treatment, not surprisingly, was aimed at encouraging the wandering organ to return to its normal position. This was done, not as one might expect by direct manual manipulation, but by luring or driving the wandering organ with various substances. Thus yellow ochre would be mixed with fresh myrrh and applied to the patient's labia, or the patient would drink a potion concocted of tar from wood from a ship mixed with dregs of beer. Alternatively ointments, made from dried excrement, would be applied to the affected parts to force the uterus to descend (Griffith 1897). Again, Merksey and Potter (1989) argue that the image of the uterus being lured or driven is an assumption on the part of Griffith and the papyrus text confines itself to describing the prescriptions not their mechanism of action.

This formulation of hysterical-like disorders held sway in Egyptian medicine and was extensively discussed in the *Papyrus Ebers* some 300 years later. This papyrus has been described as " the greatest Egyptian medical document" (Ebell 1937). It comprised of a series of monographs suggestive of a general medical textbook. The chapter *Diseases of Women* described hysterical-like symptoms extensively and its therapeutic suggestions were broadly in line with the Kahun Papryrus, if somewhat more elaborate, introducing fumigations as another means of tempting the uterus.

Although the Egyptians had a well organised hierarchical medical system which credited many vegetables, roots, fruits and resins, including senna, opium and cannabis, with healing properties, they still believed that well being was endangered by supernatural forces in addition to earthly causes (Porter 1997). They saw illness as a matter of balance. They placed as much importance on being at peace with the gods as they did with correct living. This was reflected in medical practice and prayers, incantations, amulets and exorcisms were regarded as important therapies (Veith 1965).

The clear similarities between Egyptian and Athenian medical theories indicates the spread of Egyptian ideas around the Mediterranean basin. However, it was Greek thought, not Egyptian, which was to influence medicine for the next two millenia. By far the most influential of the Greek physicians was Hippocrates. The Hippocratic school was to become the foundation of written medicine. Remarkably, despite the

seventy-two books contained in the *Corpus Hippocraticum* little is known about the 'Father of Medicine' himself. Ludwig Edelstein in the Oxford Classical Dictionary was able to describe all agreed biographical details in a paragraph.

" The Asclepiad of Cos, a contemporary of Socrates (469-399 BC), though the most famous Greek physician, is yet one of the least of all known to posterity. That he was of small stature, that he travelled much, that he died at Larissa is probable, more about his life and his personality cannot be ascertained. And as for the body of works under his name…the so-called Hippocratic books…show the most widely different attitudes towards medicine…. There is not a single book the authenticity of which was not disputed already in antiquity… It seems likely that none of the books preserved under the name of Hippocrates is genuine." (Edelstein 1970).

Scholars have argued relentlessly over how much or little of the *Corpus* was indeed penned by Hippocrates. The most sanguine view was taken by Porter (1997); the corpus should be viewed as a whole and represents the Hippocratic school and contemporary medical thought, irrespective of who actually wrote it. Hippocratic medicine, although influenced by the Egyptians was built upon a different tenet. The supernatural was explicitly rejected. This was most clear in the treatise on epilepsy *On the sacred disease.*

" I am about to discuss the disease called 'sacred'. It is not in my opinion, any more divine or more scared than other diseases, but has a natural cause, and its supposed divine origin is due to mens' inexperience, and to their wonder at its peculiar character. Now while men continue to believe in its divine origin because they are at a loss to understand it, they will really disprove its divinity by the facile method of healing which they adopt, consisting as it does of purifications and incantations. But if it is to be considered divine just because it is wonderful, there will be not one sacred disease but many, for I will show that other diseases are no less wonderful and portentous, and yet nobody considers them sacred." (Hippocrates: trans Jones1923)

The central theme of Hippocratic medicine was that health was an equilibrium and illness an upset. The body was stable until subverted by disease. The cause lay in the bodily fluids, the *humours*, blood, yellow bile, black bile and phlegm. The theory was founded upon observation of the sick. It had been noted that two of the humours, bile and phlegm, although naturally occurring, appeared to be overproduced in times of illness. Blood, by contrast, was associated with life and yet was expelled naturally from the body through menstruation and nose bleeds. Black bile was noted to be particularly harmful if found in vomit or faeces. Not only did the humours offer a system within which all maladies could be understood but they reflected other naturally occurring systems, providing a face validity to the theory. They reflected the four ages of man (infancy, youth , adulthood and old age), the four seasons, the four elements (air, fire, earth and water) and the four primary qualities (hot, dry, cold and wet) (Porter 1997).

It is generally held that the term *Hysteria* first appeared in the *Corpus*. The word was used mainly in adjectival form and applied to symptoms caused by a displaced uterus. Some historians dispute this and King (1993) claimed to demonstrate that the term never appeared in the Hippocratic texts and that it was not until much later, during the Renaissance, that it was first used. To some extent this is a semantic argument of more interest to social historians than clinicians; few would dispute that the Greeks attributed a diverse array of 'unexplained symptoms' to a uterine origin. The phenomenon was mainly considered to occur in mature woman. The hypothesis was that a lack of impregnation with sperm led to organic changes in the uterine wall. This caused the endometrium to dry up and lose weight, and then in a search for moisture rise towards the hypochondrium and beyond. The symptoms produced were dependent on the movement of the uterus. If it remained in the abdomen it impeded the flow of breath. If it rose to the heart the patient would feel symptoms of panic and begin to vomit. If it rose higher symptoms of blockage in the throat would be perceived, so-called 'globus hystericus'. On rising to the head, it would cause sensations of drowsiness and lethargy (Veith 1965).

The *Corpus Hippocraticum* also presented the earliest known case histories of hysterical mutism and paralyses.

" The wife of Polymarchus felt a sudden pain in her groin; her menses having failed to set in....She was without voice through the entire night until the middle of the next day...[and only able] to indicate with her hand that the pain was in her groin." (Hippocrates: trans Jones1923)

" Following a short and insignificant cough she developed a paralysis of the right upper limb and the left lower limb, nothing affecting the face, nothing affecting her intelligence. This woman began to improve on the twentieth day." (Hippocrates: trans Jones1923)

There was an overlap in the *Corpus* between hysterical disorders and *Diseases of Virgins.* This group of conditions was caused by the retention of menstrual blood, presumably due imperforate hymens, which created both physical and mental symptoms via pressure on the heart and diaphragm. The heart was, at the time, generally considered the seat of mental activity. Treatment was through perforation of the hymen and encouraging marriage and sexual intercourse (Hippocrates: trans Jones1923).

The Greeks observations on the aetiology of hysteria must be placed in both a cultural and a philosophical context. In ancient Greece men held superior legal status, only a son

could inherit although they were obliged to provide dowries for their sisters, sons were better educated and probably better fed, men enjoyed sexual freedom and women by contrast were not permitted to appear in public unchaperoned. Female infanticide was practiced, although it is uncertain how common it was (Pomeroy 1975). Despite this, it has been acknowledged that Athenian culture accorded more rights on women than other contemporary cultures, with equal rights of divorce and the opportunity for women of all classes to gain some exposure to art and literature via attendance at performances of the great tragedies (Badien 1975).

Woman's role in reproduction was subject to controversy and whilst Hippocrates appeared to suggest an equal role for both sexes, others, most infamously Aristotle, saw women as little more than a vessel. Athenians held that brain, marrow, spinal chord and semen were all one substance. Semen was the begetter of life and that the female role in reproduction was one of the carrier alone. The importance of semen in mens' vitality was reflected in the widespread practice of male homosexuality. Whilst it was not until the fourth and fifth centuries that Spartan aristocratic culture institutionalised homosexuality as a formal part of education and rearing of the adolescent boy, it was common and public in Athens. This form of 'educational' homosexuality was built around the belief that the virtue and strength of the older man was passed on through his semen into the anus of the young boy. Such homosexuality was seen as a preparation for manhood including the procreation of children, and social and financial penalties were placed on men who did not marry. It was intimately tied to civic education and

was governed by clear rules ensuring it was practiced, like all things in Athens, in moderation. Indeed, relationships that were too obvious or promiscuous were ridiculed (Simon 1978).

With semen being revered as the life giving force in Greek culture, its incorporation into aetiological hypotheses on uterine movement was perhaps unsurprising. Whether this hypothesis was also influenced by the position of woman in society is open to debate. Modern social historians such as King (1995) regard it as being of singular importance. She argues that "at the very heart of hysteria, we find a statement about the nature of woman and her proper social role." She cites the derivation of the word *hystera* as being related to *hysteros* (coming last) and *hysterema* (deficiency or defectiveness) (Fredriksen 1979).

The influence of philosophy was also of great importance to the origin of ideas on hysteria. Philosophers held strong influence over medical practice. Medicine was not held as the sole preserve of the physician and was included in the wider debates on human nature.

"The womb is an animal which longs to generate children. When it remains unfruitful beyond its proper time, it is discontented and angry, and wandering in every direction through the body, closes up the passages of breath, and, by obstructing respiration and

by driving them to extremity, causing all manner of disease." – *Timaeus* (Plato: trans Jowett 1894).

It must be remembered that the location of consciousness within the body was still to be decided. Both philosophers and physicians contributed to the debate. The Hippocratic school attributed the interpretation of consciousness to the brain:

" Men ought to know that from the brain, and the brain only, arise our pleasures, joys, laughter and jests, as well as our sorrows, pains, griefs and tears. Through it, in particular, we think, see, hear, and distinguish the ugly from the beautiful, the bad from the good, the pleasant from the unpleasant, in some cases using custom as a test, in others perceiving them from their utility. It is the same thing which makes us mad or delirious, inspires us with dread and fear, whether by night or by day, brings us sleeplessness, inopportune mistakes, aimless anxieties, absent-mindedness, and acts that are contrary to habit" (Hippocrates: quoted Veith 1965)

Yet, despite this emphasis on the role of the brain, they did not ascribe it independent, inherent psychological qualities. They saw it more as a mediator for air, *pneuma,* which was breathed through the mouth to the brain and was the source of intelligence and feeling (Zilboorg 1941).

Plato, the earliest writer to mention Hippocrates (Porter 1997), developed Hippocratic ideas to formulate and subsequently divide the *psyche,* a form of mind-soul (Zilboorg 1941), into three functions- reason, spirit and appetites. They were located in respectively in the brain, the heart and the liver. The highest part, reason, was seen as in conflict with the lowest part, appetite. The middle part, spirit, brought energy and passion to the aid of either (Simon 1978). Plato developed his ideas in the *Timaeus,* (Plato: trans Jowett 1894) formulating the body as built from a series of transcendental geometrical shapes constructed by the Creator with specific purpose in mind. Thus morality developed a somatic constituent; a healthy body could lead to a healthy mind. Through philosophy, medicine came to hold some juristriction on questions of morality (Porter 1997).

Aristotle, Plato's great pupil, questioned his master's transcendental ideas. He called strongly for the systematic observation of nature. Nature did nothing in vain, so body parts had to be explained in respect of their purpose. On observing embryos within eggs Aristotle perceived the beating heart as the first sign of life, and therefore located the soul there as a result of the heart's physiological primacy. The brain was 'demoted' to a role as a regulator adjusting the organism. (Porter 1997). Aristotle separated off a mind of pure reason from the body. The mind, it was implied, was unassailable by illness, the superior soul of man remained independent and supreme. (Zilboorg 1941)

This cultural and philosophical milieu allowed the uterus continued as the object of aetiological interest in hysteria. It also introduced sexual themes into the formulation. It is of interest to note that the sexual theme was very mechanistic rather than related to theories on desires and drives popularised much later by Sigmund Freud. Furthermore, despite an emphasis, by some, on the role of the brain in producing mental symptoms there was the origin of a strict mind-body divide.

These theoretical advances led to little change in the practicing physicians' techniques. The treatments of hysterical disorders recommended in the Hippocratic texts bore great similarity to those in Egyptian papyri. Therapeutic strategies were directed to inducing the uterus to return to its rightful position. The major change was the introduction of an overtly sexual element into therapeutics; the recommendation of marriage as the quickest means of achieving a cure.

Although these rationalistic approaches to disease were adopted by the Greek 'intelligentsia' it is not so clear to what extent they influenced the general population. Worship of the god of medicine, Aesculapius, was wide spread. Dreams were held to have great importance both as predictors of the future and as an aid to personal decision making. Both were combined in Temple healing, along with the power of suggestion, ritual and probably hypnotism, and this formed a popular alternative (Veith 1965).

By the time of Aristotle the glory of Athens was in decline. It was hastened by its fall in the Peloponnesian War (404 BC) and after the death of Alexander the Great (323 BC) the cultural centre moved east to Alexandria. This led to an expansion of hellenistic thought from the Persian Gulf to Sicily. Most importantly it influenced the new masters of the ancient world, the Romans (Zilboorg 1941).

Greek medicine, though, did not have an easy reception in Rome itself. The Romans saw no need for physicians, for unlike their effete Greek counterparts, they were hale and hearty (Porter 1997).

"Beware of doctors, they would bring death by medicine." (Cato: quoted Porter 1997).

However, under the influence of increasing urbanistation and hellenisation Greek medicine gradually gained acceptance. Although early writers, such as Cicero and Celsus, were educated laymen, who saw all knowledge as their provenance, they clearly held the physician to have his place.

"If philosophy could make good medical men, the philosopher would always be a better healer than the physician. The philosopher possesses only the knowledge of words, not the knowledge of how to treat sick people." (Celsus: quoted Zilboorg 1941).

Despite such comments, it was Celsus himself, and not a physician, who wrote the first medical treatise in Latin. Medical knowledge was summarised in eight volumes of a twenty one volume encyclopedia of scientific knowledge. The work was of note as it followed no particular school, and was influenced by Hippocrates and Asclepiades as well as being critical of the clashing sects of the Dogmatists, Empirics and Methodists. However, this independence did not influence his description *On diseases of the womb* and Celsus relied almost completely on Hippocratean thought:

" Females are subject to a malignant disease of the womb: and next to the stomach , this organ is highly susceptible of being affected either in itself, or by sympathy affects the rest of the body. Sometimes the affection deprives the patient of all sensibility, in the same manner as if she had fallen in epilepsia. Yet with this difference, that neither the eyes are turned, nor does foam flow from the mouth, nor are there any convulsions: there is only a profound sleep. This disease returning frequently to some females at last becomes habitual." (Celsus: quoted Veith 1965).

Roman medical thought was generally unoriginal and derivative with regards to hysteria. The one notable exception was Soranus, the most prominent of the Methodists, and an eminent obstetrician and gynaecologist. Although he still held the disorder to be uterine in origin, he rejected the idea of the womb as an animal able to wander the body. He viewed it as a disease of stricture emanating from the uterus but affecting the whole body (Veith 1965). The cure lay in relaxation for the acute phase, followed by stability

of lifestyle including regular promenades, healthy eating and passive exercise. Soranus was highly critical of Hippocrate's views on the disorder:

" The uterus does not issue forth like a wild animal from the lair, delighted by fragrant odours and fleeing bad odours; rather it is drawn together because of stricture caused by inflammation" (Soranus: quoted Veith 1965).

The hypotheses of Soranus and contemporaries were eclipsed by Galen; the medical colossus of Roman era. His prominence was as much due to his belittling of all contempories as his prolific pen. His medicine proved monumemtal, as he intended it should:

" I have done as much for medicine as Trajan did for the Roman Empire when he built bridges and roads through Italy. It is I, and I alone, who have revealed the true path of medicine. It must be admitted that Hippocrates already staked out this path… he prepared the way, but I have made it passable." (Galen: quoted Porter 1997).

Galen made a virtue of his independence of thought, considering himself not to belong to any school but to be an eclectic, his theories driven by experimental results alone.

" To what sect does Galen belong?" asked Martialis. Galen answered "He belongs to none and calls slaves all those who accept as final the teachings of Hippocrates or Praxagoras or anybody else." (Galen: quoted Sarton 1954).

Despite Galen's claim to stick to purely experimentally driven findings the philosophical instinct in him overrode the experimentalist. As his influence increased he began to transcend his experiments to expound comprehensive theories. Among these were his highly influential *pneumatic* theory of three vital spirits located in the brain, heart and liver. All physiological occurences could be explained in terms of these three *pneuma.* The pneumatic theory was to hold influence until the seventeenth century. In fact, the theory was in no sense original and obvious connections could be made with Plato's notion of the *psyche* (Sarton 1954).

It was perhaps his treatise on the *Use of parts* which was to be most influential of all. Through contemplation of the human body in all its complexity, harmony of function, mechanical perfection and unity Galen came to the idea that this could only be the result of divine Providence. He followed Aristotle in the doctrine of teleology. He rejected the notion of function helping to create the part but rather that the part has been preadapted from eternity. This was highly agreeable to later theologians of all persuasions and thus Galens praises were sung to the greater glory of God for many centuries (Sarton 1954).

Such observations made, there can be no doubt about the acuteness and accuracy of Galen's clinical observations. He noted that psychological factors could influence somatic symptoms and that mental disorders could have their cause in bodily ailments. He chided contemporaries for the lack of sophistication in this regard:

" I suppose it is because they have no clear conception of how the body tends to be affected by mental conditions. Possibly they do not know that the pulse is altered by quarrels and alarms which suddenly disturb the mind" (Galen: quoted Veith 1965)

Despite locating part of the soul within the brain in his *pneumatic* theory and the ability to observe from patients the interaction between the psychological and somatic, Galen located hysterical symptoms firmly in the uterus (Zilboorg 1941). Like Soranus, he dismissed the view of movement of the uterus. In his opinion the uterus secreted a semen-like fluid and the retention of this led to a corruption of the blood, cooling of the body and eventually irritation of the nerves. Treatment was through stimulation of the clitoris or the neck of the uterus; masturbation was in effect introduced and sanctioned as a medical treatment (King 1995).

Galen's mind was open beyond that of many contemporaries. He recognised that if retention of 'semen' led to such symptoms in women, what happened to men who abstained from sex? Clinical observation allowed that similar conditions did indeed

occur in men and he noted that they were often associated with sexual abstinence, to his mind confirming his theory. For the first time hysteria was described in men.

As the Roman Empire began to go into decline, medicine, the arts and the sciences decayed with it. In the case of medicine, the decline was hastened by a series of severe epidemics in the second and third centuries A.D. which brought chaos to the Empire and exposed medicine's limitations. At this time came the rise of Christianity offering an emphasis on charity, philanthropy, compassion for the sick and spiritual solace for all mankind (Zilboorg 1941).

Early Christianity shared much common ground with medicine but made explicit demarcations between the body and the soul. With this came the implied subordination of medicine to religion. The doctor was fit to look after the mundane 'cure' of the body but the cure of souls was for priests (Porter 1997). Christianity absorbed many differing attitudes to medicine and healing, including aspects of Eastern asceticism with its emphasis on the superiority of the soul over the flesh, and Jewish healing traditions with their emphasis on suffering as a godsend and on purification regimes. However, despite acknowledging suffering and disease as a chastisement from the Lord, the Church also promoted healing and Christ's instructions to care for the sick and needy were institutionalised (Porter 1997).

It was unclear whether such charitable views were extended to the mentally ill and those with hysteria. Whilst some sufferers were regarded as holding prophetic powers and lauded as a result, on other occasions symptoms were viewed as the work of the devil. From earliest periods of Christianity, demonologists began to study signs of possession in order to seek clarity. It was held that all those who were possessed must bear the mark so that their collaborators could recognise them. Unfortunately, for sufferers of hysteria, particular emphasis was laid on symptoms of regional anaesthesia, known as *stigmata diabolica* (Zilboorg 1941).

Of particular influence to the early church were the writings of St Augustine (354-430). Although popularly known for begging of the Lord "give me chastity and continence, only not yet" the mature man, after his conversion to Christianity, was a recluse who professed a strong aversion to sexuality and lust. Augustine wrote widely on many topics but displayed a lasting preoccupation with demonology and witchcraft and it was this concern with the ways of the Evil One that were his spiritual legacy. He, himself, was much more tentative than many of those who subsequently mis-quoted him. He acknowledged the existence of mental illness:

"We can hardly hold back our tears when mad men say or do extravagant things- things wholly unlike their customary behaviour and normal goodness" (Augustine: quoted Veith 1965).

Yet he differentiated this from:

"Still worse is the case of those possessed by demons. Their intelligence seems driven away, not to say destroyed, when an evil spirit according to its will makes use of their body and their soul." (Augustine: quoted Veith 1965).

Unfortunately his works gave no instruction on how the two states could be distinguished. However, distinguished they must be, as demonic states could only be cured by miracles, whereas disease, although obviously amenable to supernatural cures, could also be helped by medicine.

The result of this shift in the balance of thought was to alter the social attitude to the hysteric. To quote Veith:

"..and changed him [the hysteric] from a sick human being beset with emotional needs and physical distress into someone more or less wilfully possessed, bewitched, in league with the devil and even heretical." (Veith 1965).

Many historians would argue with Veith's critical view of the early era of the Church. Porter (1997) points out that despite the fact that the Church was clear that the divine was above the temporal, it was also explicit that it was man's duty to preserve life and health for the glory of God. Furthermore, although it has been easy for historians to

criticise the early hospitals for their religious ethos it must be remembered that such hospitals would not have existed at all were it not for the Church making a virtue of charity. The Benedicitine order ruled:

" the care of the sick is to be placed above and before every other duty, as if Christ were being directly served by waiting on them." (quoted Porter 1997).

Even the mentally ill and hysterics, though often viewed as possessed, were not subject to punishment. Indeed their position was one for pity and not censure. Although treatment was by prayer and exorcism, this did not carry the implications which were to come.

"I conjure thee, *O womb*, by our Lord Jesus Christ, who walked over the sea with dry feet, who cured the sick, who expelled the demons, who brought back the dead to life, by whose blood we were redeemed, by whose wound we were cured, by whose plight we were healed, by Him, I conjure thee not to harm that maid of God, N., not to occupy her head, throat, neck, chest, ears, teeth, eyes, nostrils, shoulder blades, arms, hands, heart, stomach, spleen, kidneys, back, sides, joints, navel, intestines, bladder, thighs, shins, heels, nails, *but to lie down quietly in the place God chose for thee*, so that this maid of God, N., be restored to health." (10th century prayer: quoted Zilboorg 1941).

Further evidence of humane approach to the possessed lies in the contemporary cures of the eleven and twelfth century

"In aggravated cases the actual presence of the medicinal saint was necessary; in less vexatious maladies the bare imposition of hands, accompanied by plainitive prayer, quickly healed the diseased." (quoted Zilboorg 1941).

"Wine washing [wine which had washed]...sacred objects, given to the imbicile, forcibly ejected an evil spirit from his mouth; while another tainted with idiocy was restored to instant health by simply transporting the fragments of St Anastasius." (quoted Zilboorg 1941).

5.3 The Renaissance, hysteria and the rise of the Witch Hammer.

The humane approach was to change in the fifteenth century. Pope Innocent VIII issued a Papal Bull in 1448.

"It has come lately to Our ears, not without afflicting Us with bitter sorrow,....many persons of both sexes, unmindful of their own salvation and straying from the Catholic Faith have abandoned themselves to devils, incubi and succubi, ..afflict and torment men and woman,.... with terrible and piteous pains and sore diseases, both internal and external..." (Innocent VIII: trans Summers 1928).

The bull instructed two Dominican monks Heinrich Kramer and James Sprenger to investigate. The result was the *Malleus Malificarum* (The Witch Hammer) which described their findings. It was to serve as a textbook for the examination and persecution of witches for centuries to come.

It was a great paradox that this shift in attitude came not during the heart of the Dark Ages but at the birth of the Rennaissance. As science was being reborn, Firenze was flourishing and Michelangelo was opening his eyes, the wholesale persecution of those accused of witch craft began. Indeed it was the invention of printing, one of the great contributions of the Rennaisance, that allowed it to do so. Within two centuries of the original publication of the *Malleus* no less than thirty separate editions had been printed (Sigerist 1962).

The sections of the *Malleus* of most interest to the study of hysteria lie in Part II, *Of the Way how in Particular they Afflict Men with Other Like Infirmities* and *The Remedies prescribed by the Holy Church against Incubus and Succubus Devils.*

"But who can reckon the number of other infirmities which they have inflicted upon men, such as blindness, the sharpest pains, and contortions of the body?" (Kramer and Sprenger: trans Summers 1928).

"At times also women think they have been made pregnant by an Incubus, and their bellies grow to an enormous size; but when the time of parturition comes, their swelling is relieved by no more than the expulsion of a great quantity of wind." (Kramer and Sprenger: trans Summers 1928).

Sigerist (1962) estimates that subsequent to its first appearance thousands of the mentally ill and those suffering hysteria were killed for crimes of heresy and witchcraft. Veith (1965) confidently asserts that it was beyond doubt that:

"many, if not most, of the witches as well as a great number of their victims described within were simply hysterics who suffered from partial anaesthesia, mutism, blindness and convulsions, and , above all from a variety of sexual delusions."

Leaving aside the question of whether sexual delusions were more indicative of psychotic disorders, few would go as far as her in their claims. Szasz (1961) mounted an elegantly written critique of the hypothesis that the mentally ill, and in particular hysterics, were ever mistaken for the possessed at all. He argued that many of those accused of being possessed were not ill but at odds with contemporary society and that witch-hunts could be better compared to the persecution of communists in post World War II, America. One does wonder if Szasz borrowed this hypothesis from Arthur Miller's play *The Crucible* (Miller 1953). Irrespective of the origin of the idea, Szasz was undoubtedly right in his assertion that not all accused of witch-craft were mentally

ill or suffering hysterical symptoms. Nonetheless it is very hard to accept the totality of his arguments in the face of substantive evidence from the *Malleus* itself and other contemporary treatises (Webster 1677, Jorden 1603, Hutchison 1718). There were numerous clear descriptions of persecution as a result of what would now be regarded as hysterical symptoms or psychotic illnesses. Equally clearly accusations of witch-craft were made for other purposes including personal gain and excessive zeal (Kramer and Sprenger: trans Summers 1928).

A discussion of the *Malleus* would not be complete without mention of its misogyny. The text was filled with vicious attacks on women, with chapter titles such as "*Concerning Witches who copulate with devils. Why is it that Woman are chiefly addicted to evil superstitions?*" and numerous case reports on women leading men astray, there is little doubt as to who was to emerges as the villain. In Veith's opinion the *Malleus* set women up to be the main suspects of witch hunts. By contrast, King (1987), citing linguistic evidence, suggested that women had been placed in that role, via the diagnosis of hysteria, from long before the arrival of the *Malleus*. She dates it as far back as the 8th century BC when the poet Hesiod told the tale of Pandora and how she arrived in a male world bringing with her the evils of disease, old age and hard agricultural work.

The persecution of witches in Europe reached its height in the early part of the seventeenth century. The Reformation did not stop the practice, indeed the Lutherans and Calvinists, once dubbed heretics themselves, were among the most ferocious of persecutors. Many techniques were used to detect witches but foremost was testing suspects for anaesthetic areas. *Common prickers* as they were known gave expert testimony on the examination of suspects:

"..caused John Kincaid of Tranent [near Edinburgh], the common pricker, to exercise his craft upon her. He found two marks of the devil's making; for she could not feel the pin when it was put into either of the said marks, nor did the marks bleed when the pin was taken out again. When she was asked where she thought the pins were put in her, she pointed to a part of her body distant to the real place. They were pins of three inches in length." (Pitcairn: quoted Veith 1965).

Acceptance of witchcraft as the explanation for myriad of bizarre presentations was not altogether complete. Johan Weyer, a pupil of Cornelius Agrippa, published *De Praestigiis Daemonum* (On the Trickery of Demons) in which he defended women who had been accused of being possessed or of sorcery. He argued that the effects of the devil were mediated by an accumulation of black bile in the brain. He repudiated the existence of witchcraft and offered a medical explanation as an alternative. The important effect was to reason that the woman were not criminal but sick, be it spiritual or physical, and therefore deserved of pity. (Zilboorg 1941)

By the end of the seventeenth century, there was a general realisation of the role of suggestibility and the power of narrative in explaining some of what had happened. Among the most influential early critiques was John Webster's *The Displaying of Supposed Witchcraft.* He noted the power of suggestibility and the ease with which people were influenced:

"Some are as much in love with the brood of their own brains, as others are with the fruit of their loines." (Webster 1677).

"There are actions in most of those Relations ascribed to Witches, which are ridiculous and impossible in the nature of things; such are (1) their flying out of windows, after they have annointed themselves, to remote places. (2) Their transformation into Cats, hares and other Creatures. (3) Their feeling all the hurts in their own bodies which they have received in those. (4) Their raising Tempests, by muttering some nonsensical words or performing ceremonies alike impertinent as ridiculous, And (5) their being suck'd in a certain private place of their bodies by a Familiar. These are presumed to be actions inconsistent with the nature of Spirits, and above the powers of those poor and miserable Agents. And therefore the Objection supposeth them performed onely by the Fancy; and the whole mystery of Witchcraft is but an illusion of crasie imagination." (Webster 1677).

This was followed some fifty tears later by The Reverend Francis Hutchison's *An Historical Essay concerning Withcraft*. Hutchison, the Chaplain in Ordinary to His Majesty recognised the role of suggestibility and the influence this could have on the clinical presentation of hysteria

"Natural Fits and Vapours [hysteria], for when some sort of Fits which are undoubtedly Natural continue, they alter the Habit of the Body… and then their Fancies and Symptoms are most surprising. There are marvelous Effects both in their Minds, Eyes, Ears and Voices." (Hutchison 1718).

Hutchison had clearly been influenced by the recent events in New England. In Salem, as a result of an atmosphere of intense suspicion, created by the knowledge of witch trials in Great Britain, there crystallised an outbreak of mass hysteria in which nineteen people, including children, confessed to, and were subsequently being executed for, witchcraft (Veith 1965).

5.4 From the uterus to the brain.

Despite the sixteenth and seventeenth century seeing hysterics tortured and put to death as a result of their symptoms, they were also a time of great advancement in the understanding of the disorder. Through this period there was a gradual transition as hysteria moved from the uterus to the brain. Porter (1997) describes the early years of the Renaissance as a time when medicine needed a fresh start from its stultifying

homage to antiquity. At the vanguard of such a desire was Paracelsus. He proclaimed that " my shoe buckles contain more wisdom than both Galen and Avicenna." His doctrine was that nature was sovereign and that the healer's duty was to know her and obey her. He professed great belief in folk wisdom and dabbled in chemistry linking elements to astrology. He was unequivocal in rejecting demonology as an explanation for mental disorders which he viewed as a natural disease of the *spiritus vitae.* His insights upon hysteria were somewhat mundane; he regarded it as a disease of uterus. However, he developed his own theory of uterine cramps and contractures in response to a build up of acid within the womb as the mechanism of action (Zilboorg 1941). It was his observations on *St Vitus Dance* which were of most interest, although modern understanding of movement disorders would question his veracity.

" thus, the cause of the disease chorea lasciva is mere opinion and idea, assumed by the imagination, affecting those who believe in such a thing. This opinion and idea are the origin of the disease both in children and adults.....unconsciously they have fantasies about what they have seen or heard." (Paracelsus: quoted Sigerist 1941)

In this passage Paracelsus outlined the first description of unconscious motivation in disease presentation. His ideas, though, remained largely ignored for the next four centuries; perhaps in part due to his irreconcilable nature.

Johannes Weyer was everything Paracelsus was not: a gentle, humble, methodical man. In his work *De Praestigiis Daemonum*, he developed the role of suggestibility in the aetiology of hysterical symptoms and was also forthright about the disability caused to the patient by their symptoms.

"but it [the imagination] receives unto itself the images of all things; it fashions and represents all the activities of the mind and adjusts outside things to those within....it brings out fantasies which go much further than the senses; it goes beyond any senses..... like a chameleon" (Weyer: quoted Zilboorg 1941).

"Can you think of a misery anywhere in the world that is worse than theirs? If they do seem to merit punishment , I assure you, their illness is enough alone." (Weyer: quoted Zilboorg 1941).

Despite his championing of the mentally unwell and achieving a certain notoriety as a result of criticism of his views by Jean Bodin, Weyer remained relatively non influential until over a century after his death.

The major contribution Paracelcus, Weyer and others was to deny supernatural causes of disease and return medicine to a Hippocratean stance. They also recognised the role of the imagination and suggestibility in the expression of disease. In the process of their descriptions they paved the way for a major theoretical shift in the understanding of

hysteria. They did not however discuss the condition in detail themselves and their contributions were implicit rather than explicit. Their views and in particular their willingness to challenge the accepted wisdom was to be built upon by others.

After having given medical evidence in a sorcery trial Edward Jorden, an English physician, wrote *A Brief Discourse of a Disease Called the Suffocation of the Mother* in the hope that by aquainting both the public and the medical profession with nature of the disorder hysterics would never again be mistaken for the possessed. In his text Jorden linked commonly held Platonic ideas of a tripartite soul with his own theory on the uterus producing noxious substances. These *vapours* interacted with the brain and occasionally the liver to produce symptoms (Jorden 1603). Thus the *vapours* interacted with the *animal faculty* allowing disorders of the imagination, memory, reason and the senses. They also interacted with the *natural faculty* to cause digestive problems.

This uterine/brain theory was continued by Burton in the *Anatomy of Melancholy*; it should be noted that the term melancholy in the seventeenth century bore little resemblance to its current use (Berrios 1988). Hysteria was described under the name of *Maids, Nunns, and Widows Melancholy.* Burton hypothesised that the uterus was still the seat of the disorder but that the brain was involved by consent:

" The causes are assigned by Hippocrates...offended by those vicious vapours which come from menstruous blood..... the whole malady proceeds from that inflammation,

putridity, black smokey vapours, &c., from thence comes care and anxiety, obfuscation of spirits, agony, desperation and the like." (Burton1676)

He also recognised that with emotional distress came physical symptoms and in describing *Windy and Hypochondriacal Melancholy*:

" ...besides fear and sorrow, sharp belchings, fulsome crudities, heat in the bowels, wind and rumblings in the guts, vehement gripings, pain in the belly and stomack" (Burton1676).

The expansion of Jorden and Burton's ideas led to the first clear statement, by French physician Carolus Piso, that hysteria was a brain disorder. This conclusion was followed by the logically connected belief that it must therefore be a disorder of both men and women:

" We believe we are correct in concluding that all the hysterical symptoms....have been attributed to the uterus...for the wrong reason. All come from the head. It is this part which is affected not by sympathy but ideopathically" (Piso: quoted Veith 1965)

With the development of the fledgling specialty of *neurologie*, hysteria was to become firmly associated with the nervous system. Thomas Willis, accredited by many as the

founder of neuroanatomy and neurophysiology, sought to confirm the brain as the seat of hysteria:

"..as we have shown before the passions vulgarly called hysterical do not always proceed from the womb, but often from the head's being affected: so though it has been vulgarly held that the affects called hypochondriacal are caused for the most part by Vapours arising from the spleen, and running hither and thither; yet in truth those distempers are for the greatest part convulsions and contractions of the nervous parts." (Willis: quoted Veith 1965).

Within the context of hysterical disorders Willis described symptoms such as pain, flatulance, indigestion, tremblings, palpatations, cramps and numbness. He demonstrated that only the nervous system could be responsible for causing symptoms in so many disparate body parts. Although some continued to expound upon the uterine origins of such symptoms until well into the nineteenth century, it was with the work of Willis that the shift to neurological explanations was made. His other assertion, that males could, in effect, have hysteria was in many ways more radical and one that the world was much less sympathetic to. However, Willis did not completely abandon the theories of antiquity. Instead he brought them together with modern views on mechanical man and proposed that [Galenic] '*animal spirits*' acted upon the nervous system to create hysterical symptoms. In Willis' theory the *spirits* exploded in the middle of the brain to cause hysterical symptoms:

"to wit that the spirits inhabiting it being disposed to explosions, and there being exploded, bring on or cause every Falling Evil." (Willis: quoted Brain 1963)

Willis's view of mechanical man had been profoundly influenced by Rene Descartes. Descartes had cast himself in the role of a doubter and set out to define a system of natural philosophy starting from first principals. He determined that the only fact that could be fully relied upon was his own sensation of consciousness; *cogito, ergo sum,* I am thinking, therefore I exist. He taught that mind was an insubstantial, immortal seat of consciousness and body, by contrast, was a machine to be explained physiologically in terms of matter and motion. Descartes moved away from the Platonic idea of a tripartite soul to a unitary concept. Although he rigidly segregated mind and body, Descartes always insisted upon substantial union between the two. This led to the intriguing proposition that while thought itself did not originate in the nervous system, disorders of thought could be caused by disordered mechanics within the nervous system. The senses, memory, imagination and judgement were developed from mechanical processes whereby particles, the *animal spirits*, in the blood entered into the brain following rarification by the heat of the heart. In this model the nerves were conceived of as hollow tubes which would allow passage of the *spirits* around the body. Memories were created by traces of these spirits being left in the brain. (Wright 1980)

This mechanistic view of man was developed, in relation to hysteria, by Thomas Sydenham; the 'English Hippocrates'. With Sydenham came the classification of groups of symptoms into diseases. He followed Descarte's theories of mind being strictly separated from body, yet declared that:

"[in hysteria]..the mind sickens more than the body." (Sydenham: trans Latham 1848)

He too favoured a direct causality of *animal spirits* acting on the brain to cause symptoms. Unlike Willis he did not regard this to be the result of explosions but rather due to the delicacy of the framework of the mind itself:

"a structure consisting in the harmony of eminently excellent and almost divine faculties; so, whenever the constitution of the same shall, by any means, have become interrupted and broken down, the ruin will be great." (Sydenham: trans Latham 1848)

"it is from the irregularity of the spirits that the inconsistency both of mind and body....so prevalent with both the hysterical and hypochondriacal take birth.....the spirits which are at the top of the scale of matter, and on the very verge of immaterial entity." (Sydenham: trans Latham 1848)

It was with Sydenham that hysteria began to become a disease not of the brain but of the mind. This distinction was of vital importance, Aristotle, had declared the mind

supreme and unassailable by illness and this was echoed by Descartes, yet Sydenham implies that via weakness in the structure of the brain it was the mind that became sick. One might hypothesise that it was with this distinction that a negative attitude towards suffers of hysteria began (for suffering from hysteria itself, rather than because they were mistaken as witches). Certainly Sir Richard Blackmore writing some fifty years later reports that:

"patients are unwilling their Disease should go by its right Name…[because they think it implies their symptoms]…imaginary and fantastick Sickness of the Brain, filled with odd and irregular ideas…[such patients]…become an Object of Derision and Contempt…[although Blackmore, himself, considered]… Sufferings are without doubt real and unfeigned." (Blackmore 1725)

Sydenham recognised hysteria and hypochondriasis to be the same disorder, "as alike as one egg to another". He commended the study of the disorder to other physicians for he believed it to be the commonest chronic disease and the ultimate test of a physician's skill:

"The frequency of hysteria is no less remarkable than the multiformity of shapes which it puts on. Few of the maladies of miserable mortality are not imitated by it. Whatever part of the body it attacks, it will create the proper symptom of that part. Hence, without skill and sagacity the physician will be deceived;" (Sydenham: trans Latham 1848)

Whilst insisting on patients' sanity, "it is neither the maniac or the madman that we write about", Sydenham recognised an emotional component to hysteria. He considered this to be secondary to physical suffering and bodily torment and not of aetiological significance. Nonetheless, he gave detailed descriptions of both depressive symptoms and [what would now be referred to as] histrionic traits within the context of the disorder

"All is caprice, they love without measure those whom they will soon hate without reason..... Again almost all of the hysterial women that I have ever seen complain of dejection (a *sinking* they call it of the spirits; and, when they wish to show where this contraction (or *sinking*) exists they point to the chest" (Sydenham: trans Latham 1848)

Therapeutically, Sydenham was reminiscent of the Hippocratean philosophy. He recommended conventional measures to purify and fortify the blood and regular exercise for its beneficial effects. Interestingly, he also comments on the phenomena of extreme sensitivity, of patients with unexplained symptoms, to side effects of medication:

"Some females have so peculiar an idiosyncracy as to feel an absolute repugnance to all so called hysterical medicines...omit them entirely....with nature against us all is in vain." (Sydenham: trans Latham 1848).

Sydenham's influence, and thankfully his humane approach to treatment, Willis by contrast advocated beating patients with a stick, had a lasting effect. This was in part because his ideas and methods were advocated by Giorgio Baglivi who was appointed by Pope Clement XI to the chair of Medical Theory in the Collegio della Sapenzia in Rome (Porter 1997). Baglivi wrote at length on hysteria modifying Sydenham's views by suggesting that emotional symptoms were not secondary to the physical symptoms of hysteria but causative of them. Baglivi advocated exercise and change of social circumstances to try to effect a cure. Furthermore, he encouraged physicians to enquire about the patient's mental state and to try to instill hope and optimism (Veith 1965).

5.5 The Enlightenment and stigmatisation.

The eighteenth century, the Age of Enlightenment, brought with it contrasting views on hysteria. Aetiological hypotheses would be challenged from within medicine but also by newly developing ideas from fields outside of medicine. At the forefront of the new thinking was Isaac Newton, whose experimental *Principia* offered a persuasive, testable scientific way of viewing the world. Newton was worshipped by the scientific community and attempts were made to incorporate his thoughts into an understanding of medicine in terms of weights and measures, forces, and hydrostatic pressure. Herman Boerhaave, Professor at Leiden University and the most famous physician of the day, was particularly influenced by Newton. He attempted to explain all disease in terms of hydrostatic equilibrium, a balance of internal fluid pressures he termed

Corpuscularian Matter Theory. Boerhaave's hydraulic model was initially highly influential. However the rapidly accumulating physiological knowledge basis shifted attention from the vascular to the nervous system (Porter 1997, Zilboorg 1941).

It was one of Boerhaave's pupils, Scottish physician Robert Whytt, who was partially responsible for returning attention back to the nervous system. Whytt published his theories in a treatise *Observations on the Nature, Causes, and Cure of those Disorders which have commonly been called Nervous, Hypochondriac, or Hysteric.* In his work, as a result of concern regarding the widespread and differing uses of terminology, he echoed Sydenham and sought to clarify what was actually meant by a *nervous* disorder.

"since in almost every disease, the nerves suffer more or less, and there are very few disorders which may not, in a large sense, be called nervous, it might be thought that a treatise on nervous diseases should comprehend almost all the complaints to which the body is liable..... [but hysteria and hypochondriasis]...in a peculiar sense deserve the name nervous...owing to an uncommon delicacy or unnatural sensibility of the nerves, and are therefore observed chiefly to affect persons of such a constitution." (Whytt 1765)

Whytt, through work in the dissecting rooms, had shown nerves to be predominantly solid and not hollow as was previously believed. This led him to doubt the idea of animal spirits travelling in the nerves and also to conclude that nerves did not activate

muscle tissue by a hydraulic system. Rather, he hypothesised that *sympathy*, a term for how bodily components came to be co-ordinated (Berrios and Mumford 1995), was based on the network of nervous tissue and was thus ultimately a function of the brain. A disorder of *sympathy* would therefore bring about bodily symptoms, although the mechanism eluded him.

"Nothing makes more sudden or more surprising changes in the body, than the several passions of the mind. These however, act solely by the mediation of the brain, and, in a strong light, shew its sympathy with every part of the system." (Whytt 1765)

Out of the ideas of both Boerhaave and Whytt came William Cullen's highly influential classification system. The system was developed from botanical classifications and divided diseases into geni and species. Within this context, Cullen sought, like Boerhaave, to explain all diseases in a unified mechanical hypothesis. However, under the renewed interest in the nervous system, generated by Whytt and others, he centered on it and not the blood. He failed to heed Whytt's warning on specificity and formulated that all diseases were caused by varying tonus within the nervous system and finite supplies of energy within the brain (Cullen: edited Thomson 1828). In general, tone was either diminished or excessive. The term *neuroses* was coined to describe disorders of sense or motion, without original fever or local disease. Neuroses were caused by either spasm or atony of the nerves and included such diverse disorders as rabies, epilepsy, hysteria, and delusional disorders but not hypochondriasis (Cullen: trans Lewis 1807).

Within this classification of disease Cullen reverted to ancient wisdom and reestablished the link of hysteria with the uterus, but unfortunately never really explained how this related to its causation as a spastic disorder of the nervous system:

"that physicians have at all times judged rightly in considering this disease as an affection of the uterus and other parts of the genital system." (Cullen 1796)

Although such mechanistic views of man were pursued throughout the Enlightenment, it was a time of controversial theories. Many alternative and contradictory hypotheses were propagated. George Ernst Stahl, in his doctoral thesis *De Sanguinificatione,* argued strongly against the theory of *animal spirits* and ascribed the circulation of blood to a *soul*. This was not a spirit but a special force, a drive characteristic for every living organism. Stahl, in effect, linked man with the beasts and thus separated living matter form non-living matter, as opposed to separating man from all other matter as previous theories, including Descartes, had. This theory was to influence his views on mental disorder and, at a time when Cartesian dualism was becoming increasingly influential, he argued passionately against a mind-brain dichotomy. He held that the life-force was responsible for all functions of a living organism and that mental disease would occur when the life-force or soul was impeded in its function. This inhibition was frequently due to mood or ideas contradictory to the driving soul. Stahl ideas were particularly influential in France where Bouissier de Sauvage, Barthez and Pinel were receptive to them (Zilboorg 1941).

The Enlightenment was to see a rise in interest in unconscious thought, predominately through the work of philosophers. Berkeley described "imageless thought" although he rejected its importance. Hume in developing his views on the "blending" of perceptions conceptualised *impressions* and *ideas* as basic forces of mentation and activity. His work started to conceptualise the idea of mental activity occurring at a non-conscious level (Zilboorg 1941). The dominant thinker of the era was Immanuel Kant. He claimed the territory of mental disorders for the philosopher alone and rejected the role of physicians altogether. Kant in a sense preempted the development of cognitive behavioural theories describing "certain internal sensations which are not the expression of real disease cause nonetheless great anxiety about having one." He went on to explain that humans have the characteristic of magnifying a sensation by concentrating upon it (Kant 1800). Kant called attention to the state of primitive man who was healthy "because he is free in his movements." Or, if man is not subject to the demands of the environment nor, owing to the influence of drives and needs, subject to frustration, he too will be healthy (Berrios and Mumford 1995). In this concept one can determine a move towards the ideas of the unconscious developed by the psychoanalytic schools. One can also see, particularly within Stahl's work, the origins of Freud's view on neuroses and Ferenczi's pathoneuroses (Zilboorg 1941).

Dualistic/mechanistic views of nervous tissue with separated inviolate souls, and more monist paradigms with the concept of unconscious thought, characterised the

dichotomous theories developed on MUS during the Enlightenment. However, it was two other events at the end eighteenth century that were to have a defining effect on the understanding and attitudes towards those perceived as mentally ill. In 1788 King George III had his first episode of insanity. His physicians-in-ordinary proved unable to help and his care was entrusted to Revd Dr Francis Willis, a clergyman who ran a madhouse in Lincolnshire. Willis recommended calm and control. His 'moral management' involved both physical restraint, including straight jackets, gags and a restraining chair, and force of personality. When the King recovered, from what is now hypothesised to have been acute intermittent porphyria, Willis took the credit. This confirmed the use of physical treatment in the insane but also, and of more importance theoretically, suggested a deficit of understanding rather than a disease of body or soul (Porter 1997).

Such *moral* treatment influenced the work of Phillipe Pinel (Pinel 1808). He too viewed insanity as a disorder of understanding:

"Derangement of understanding is generally considered as an effect of an organic lesion of the brain, consequently as incurable; a supposition that is, in a great number of instances, contrary to anatomical fact." (Pinel 1808)

This led him to define both *moral* (functional) and *physical* (organic) forms of insanity. He recommended humane treatment and is famously, if with some embellishment over

the course of history, depicted as striking the chains of the insane. His therapies involved physical labour and the instillation of optimism through force of personality. Pinel discussed hysteria under the heading of *Genital Neuroses of Women*. In addition to suggesting the disorder was functional and did not involve pathological lesions, Pinel echoed Galen in suggesting that sexual deprivation was of aetiological significance. He also considered sexual excess, including masturbation, to be an equal risk. He influenced the beginnings of the conceptualisation of disorders of function within the nervous system and reawakened a dormant interest in sexuality. His theories implied that sexual drives as well as actual behaviour were of importance.

Pinel was not the only man with radical ideas to arrive in Paris in 1778. Anton Mesmer came, under a cloud from Vienna, to "take Paris by storm" (Zilboorg 1941). In his doctoral thesis Mesmer claimed to have made the ultimate discovery that a Newtonian aetherial fluid, *animal magnetism*, was "permeating the entire universe and infusing both matter and spirit with its vital force", disease came when obstructions prevented the free flow of fluid within the body (Porter 1997). Mesmer applied magnets to affected parts in order to remove the obstructions and return the body to health. Initially, he had very successful results and his departure from Vienna seems in part influenced by professional jealousy (Veith 1965). On arriving in Paris, Mesmer moved to group treatments in a *baquet*; a large tub with iron rods and mirrors, which appealed to Parisian tastes. In a séance-like atmosphere, Mesmer would, with his Magnetic wand, stroke people until they had curative convulsions (Zilboorg 1941). Several

commentators have alleged sexual impropriety during the process (Veith1965). Concern about the practices of Mesmer and his followers led the *Académie des Sciences* set up a five-member committee to investigate the practice and effects of magnetism, it included Benjamin Franklin and Dr Guillotin. Their report was extremely damning:

"The committees, aware that the magnetic fluid could not be noticed by any of our senses, that it had no effect on the members of the committees, nor on the patients who were submitted to it; having assured themselves that the touchings and the pressures cause changes rarely favourable to the animal economy and disturbances always harmful to the imagination……unanimously concluded…that such [animal magnetic] fluid does not exist and therefore cannot be useful." (quoted Zilboorg 1941).

Mesmerism did not disappear altogether, it was endorsed by Pinel as useful for women, although never for men, and continued to enjoy enthusiastic support in Britain. However, there were many sceptics, among them was a Scottish surgeon James Braid, who, nonetheless, became increasingly interested in the phenomena. He began to realise that the paraphernalia of magnetism was not central to the effects produced. He was able to obtain similar results using the power of suggestion alone. In particular he was able to produce a trance like state, *neuro-hypnotism*, a "phenomena… induced solely by an impression made on the nervous centres." He wrote his findings up in a monograph *Neurypnology; or the Rationale of Nervous Sleep, Considered in Relation with Animal Magnetism*. Baird was very careful to dismiss all reference to Mesmerism least his

discoveries by subject to allegations of quackery. He was also cautious in regard the applicability of the treatment:

"I feel quite confident we have acquired in this process a valuable addition to our curative means; but I repudiate the idea of holding it up as a universal remedy; nor do I even pretend to understand, as yet, the whole range of diseases in which it may be useful. Time and experience alone can determine this question, as is the case with all other new remedies." (Baird 1843).

Despite his rigour, Baird was still subject to criticism by the French *Académie des Sciences*. He fought back vigorously and reminded them that their committee had also criticised Harvey's discovery of circulation as a fallacy. His protestations fell on deaf ears and his views remained unaccepted, particularly in France where those who expressed any interest still believed that it was magnetic fluids that caused transmission. Most remarkably such a belief in magnetism was upheld by Jean-Martin Charcot the most precise neurologist of the day.

The first half of the nineteenth century saw several other significant developments. Medical Psychology began to emerge as an exciting new specialty. At the forefront was Baron Ernst von Feuchtersleben. In his book *The Principles of Medical Psychology* he outlined the terms *psychosis* and *psychiatry* in their current sense. The book was so influential that the Sydenham Society bestowed on it the unique honour of having it

translated whilst the author was still alive, breaking their usual tradition "that the stream of time should flow over them [books]" in order to ensure their quality. Von Feuchtersleben was born to an aristocratic background in Vienna and a career in medicine was viewed as a somewhat humble choice for a man in his position. His independent spirit showed in his work, particularly in his exploration of *unconscious language*, although he, himself, acknowledged a great debt to the ideas of Stahl and Kant. He viewed hypochondriasis and hysteria as transitory conditions between health and sickness brought about by abnormal interpretation of sensory material.

"hypochondriasis, as a state of disease, whose reduction to one principle, and whose treatment have always been the *vexa medicorum* is in essence nothing but a coenaesthesis abnormally heightened in all directions"

Von Feuchtersleben described two forms of the disorder depending upon whether the coenaesthesia originated from psychological heightening, via persistent selective attention, or from an organic increase in the sensitivity of the nerves. He noted "in nature, however, there appears to be a circle between psychical and physical cause.

He also commented upon psychogenic predispositions to hysteria which he noted to depend on many factors but particularly sexual frustration:

"and in whom both the want of exercise in those sexual functions intended by nature for use and disappointed desire or hope, or at least the feeling of having failed in their earthly destination are to be taken into account."

Whilst von Feuchtersleben was outlining some of the theories which were to be developed and made famous by Freud, Germanic science was also taking another parallel path. Wilhelm Greisinger severed all links with philosophy and espoused a very different ideal.

"Psychiatry and neuropathology are not merely two closely related fields; they are one field in which only one language is spoken and the same laws rule." (Greisinger: trans Robertson and Rutherford 1867).

While von Feuchtersleben looked for psychological explanations for hysteria Greisinger searched for somatic answers. However, he was not sure if mild cases of hysteria were even a mental disease. He recognised that there was spectrum of disorders being described and also that there was an overlap between personality and physical symptoms. He saw milder forms of the disorder as willful misdemeanours compared to the somatic form of "serious hysterical mental disorders" (Greisinger: trans Robertson and Rutherford 1867).

Much of the difference between the two men's views stemmed from whether displayed symptoms were due to cause or effect. Both saw and commented on aspects of patients' personality, in particular sensitiveness, irritability and ego-centricity. In addition, both recognised erotic elements to many patients' presentations. The essential difference was that Greisinger viewed all these symptoms as secondary phenomena to an underlying brain disease whereas von Feuchtersleben thought they were primary and causal. In many ways they represent the parallel directions in attempts to understand the functions of the brain/mind during this era, both were gifted observational scientists but both made radically inferences as a result of their observations and theoretical beliefs.

Although the area of sexual drives was emphasised in the genesis of hysteria by both the psychological and somatic camps it was always in quantitative terms, patients were described as having excessive desires or pathological lack of interest. This was to change with an initially obscure text, *On the Pathology and Treatment of Hysteria*, by Robert Carter. Later in his career Carter was to achieve great fame, both as an opthalmological surgeon and as a war correspondent with the *Times* and the *Lancet*, but at the time of writing Carter was an unknown twenty five year old general practitioner in a rural district of England. The work was singular because it described sexual desires and passions not in terms of quantity but emphasised that the qualitative experience was of more importance. In particular, he described the repression of emotions as potentially pathological:

"And, therefore, it is reasonable to expect that an emotion, which is strongly felt by great numbers of people, but whose natural manifestations are constantly repressed in compliance with the usages of society, will be the one whose morbid effects are most frequently witnessed. This anticipation is abundantly borne out by the facts; the sexual passion in women being that which most accurately fulfills the prescribed conditions, and whose injurious influence upon the organism is most common and familiar. Next after it in power, may be placed those emotions of a permanent character, which are usually concealed, because disgraceful or unamiable, as hatred or envy; after them others equally permanent, such as grief or care, but which not being discreditable, are not so liable to be repressed." (Carter 1853)

Within the context of hysteria Carter emphasised a three stage process: the primary attack which was convulsive, secondary attacks which followed recollection of associated emotions and tertiary attacks which could be brought on at will. Patients who displayed the tertiary form were, therefore, seeking attention, they displayed "selfishness and deceptiveness allied", and were not victims of sexual frustration. He recommended that treatment should be *moral* (psychotherapy) and that particular attention should be paid to emotional life of the patient and womens' *moral obliquity* (Carter 1853).

With the tertiary attack, and its suggestion of feigning, came more punitive therapies. The famed gynaecologist Alfred Hegar recommended oophrectomy for severe hysterics

and Nikolaus Freidrich advocated cauterisation of the clitoris as an effective treatment. Jules Falret summed up the new attitude to hysteria when he declared:

"These patients are veritable actresses; they do not know of a greater pleasure than to deceive" (Falret 1890).

As the psychologists and the somaticists struggled in Europe, a similar debate was taking place in the United States. In 1869 fashionable New York neurologist George Beard and the somewhat unfashionable Kalamazoo psychiatrist Van Deusen made simultaneous claims to have described a new condition *neurasthenia*. The struggle between neurologist and psychiatrist mirrored the wider professional struggle between the two schools in the United States at the time; in both contests neurology won (Wessley 1995). Neurasthenia was characterised by overwhelming physical and mental fatigue. However, it was a broad church and allowed depressed mood and a hotch-potch of physical symptoms to also be included. It was recognised that the disorder was not new and that Beard owed a debt to *hypochondria*, *neurospasm* and *spinal irritability* (Arndt 1892). Beard like many before him used contemporary scientific thought to explain his findings in terms of electrical nervous impulses, electricity and the reflex spinal arc (Beard 1881). Wessley (1995) considers the key to Beard's success was that "he articulated his ideas to a receptive audience". Beard certainly emphasised the social standing of his patients and placed neurasthenia in the social context of contemporary changes in society and the problems of *modern civilisation* (Beard 1880). The picture

was of the hard pressed business man overdrawn on nervous capital, it was made clear that the diagnosis was exclusive and reserved for the elite of society only. Those that suffered, agreed with Marcel Proust, and regarded themselves as having special understanding in "cerebral and nervous matters" (Proust 1983). Indeed, "the world would never realise how much it owes to them [neurasthenics], and what they have suffered in order to bestow their gifts upon it." (Proust 1983). Initially neurasthenia was well received by the medical profession, not least because of the large sums in private fees they brought with them. However, following its initial boom, the illness began to be described among the lower social classes and among women (Savill 1906). Soon after the disorder began to lose both its prestige and its organic aetiology:

"..remarkable changes in nerve cells....were highly fashionable and a matter of pride to both patient and diagnostician.. but could not be replicated. Fatigue exhaustion is no longer tenable" (Meyer: ed Winters 1962).

"[neurasthenia is] a state of habitual valetudinarianism with no corresponding characteristic organic lesion." (Tanzi 1909).

With this change in accepted aetiology and status it was not long before the disorder became discredited both by patients, who didn't want to be labeled with it, and doctors who didn't wish to study it (Wessley 1995). It was described in terms of "dump-heap" (Browning 1911) or "waste basket" (Kinnear Wilson 1913).

Corresponding with the change in view on the disorder came an altered attitude to treatment. Initially measures to replenish the body's stores of energy were advocated, but as an increased belief in a psychological aetiology developed so the accepted management became psychotherapy and, in particular, psychoanalysis. One of the great paradoxes, was the misjudgement with which history has viewed Weir Mitchell's supposedly "organically" based rest cure:

"to lie abed half the day, and sew a little and read a little, and be interesting and excite sympathy, is all very well, but when they are bidden to stay in bed a month, and neither to read, write, nor sew, and to have one nurse,- who is not a relative,- then rest becomes rather a bitter medicine, and they are glad enough to accept the order to rise and go about when the doctor issues a mandate which has become pleasantly welcome and eagerly looked for." (Mitchell 1877).

Indeed, far from being an attempt to dominate women or a misguided effort to rectify "cerebral energy", the cure is, in fact, a paradoxical intervention of some psychological sophistication. Not only did Mitchell cause patients to actively dislike bed rest and take up exercise in the longer term, but he did it in a way that did not humiliate them in the process. Patients showed their support of Mitchell's treatment strategies by giving him an income of $70 000 per annum (Wessely *et al* 1998).

5.6 The Salpêtrie, suggestibility and sexuality.

France, in the second half of the nineteenth century, was to see the golden era of hysteria research. During this period over 300 doctorates were conducted on the subject. Foremost, was Paul Briquet's *Treatise on Hysteria* (Briquet1859), a clinical and epidemiological study of 430 patients seen over a ten year period in the Hôpital de la Charité. Briquet gives an estimate of the prevalence of the disorder which, with the notable exception of Sydenham's work, had been lacking. In his hospital just under a quarter of females, at any one time, had hysteria with a further quarter having hysterical traits. The age of onset was characteristically young. He described several factors which predisposed to hysteria. Contrary to universal opinion he noted it to be more common among the lower social classes. He demonstrateded an association with childhood abuse. He found that it arose from situations of grief, worry, jealousy and fear but never joy happiness or pleasure. Finally, by comparing, rates in nuns, servants and prostitutes, he concluded that sexual abstinence was not a risk factor, and if anything was protective. He also noted a series of immediate precipitants which were mainly traumatic life events. He described a range of symptoms which, in modern classification systems, would correspond with somatisation disorder rather than conversion disorder. Briquet held the condition to have a poor prognosis (Mai and Merskey 1980).

The work of the illustrious Jean Martin Charcot built upon Briquet's thesis (Marsden 1986). Whilst Veith (1965) criticises Charcot's contribution as a "tragedy" owing to his misguided confidence in aspects of hypnotism, to most others he remains one of the

great neurologists. Charcot, in fact, did not start out as a neurologist but wrote his doctoral thesis describing the clinical separation of gout from chronic rheumatoid conditions. He developed his neurological interest at the age of 37 after being appointed as a physician at the Salpêtrière Hospital, where he inherited the legacy of Pinel. It was his descriptions of multiple sclerosis, the tabetic arthropathies, amyotrophic lateral sclerosis and the localisation of lesions of the spinal chord that caused his rise to fame as the pre-eminent clinical observer (Bailey 1959). As a result of an administrative change at the Salpêtrière, wards were closed down and a group of patients with hysteria and a group with epilepsy were separated off from the insane and cared for within the same ward. Charcot was struck that the epileptics were largely unchanged by this move but the patients with hysteria started to mimic the epileptics and before long were displaying all the signs of epilepsy. Charcot originally thought that the move had engendered a new condition but came to realise that it was suggestibility that was the key to this change (Charcot: trans Sigerson 1877). Charcot noted that the word hysteria "meant nothing", by which he meant there was no link to the uterus, and that men as well as women could develop the disease, which he saw as a neurosis, a disorder of function of the nervous system, which had both periodic attacks and permanent stigmata (Marsden 1986).

"There is without doubt a lesion of the nervous centres but where is it situated and what is its nature? It is I opine [in the case of a hysterical upper limb paralysis], in the grey matter of the cerebral hemisphere on the side opposite the paralysis, and more precisely

in the motor zone of the arm... but certainly it is not of the nature of a circumscribed organic lesion of a destructive nature... We have here unquestionnably one of those lesions which escape our present means of anatomical investigation, and which for want of a better term, we designate dynamic or functional lesion." (Charcot: quoted Trimble 1982)

Nonetheless, as the Salpêtrière only admitted females, that was the patient group he saw and, slightly at odds, with his observations he began to view the areas around the ovaries and breasts as *hysteriogenic* and recommended treatment with an ovary compressor. In fairness to Charcot, his reputation was as an observational scientist not as a treating physician and one should, perhaps, not attach much importance to the strategies he recommended.

Charcot differed from previous writers who had echoed Sydenham's view that hysteria was the great "chameleon" of medicine (Sydenham: trans Latham 1848). Charcot, by contrast, claimed that all hysterical attacks followed the four stages he had described in hystero-epilepsy (Veith 1965). However, he did acknowledge that some hysterics did not have convulsions and he made the distinction of major hysteria, which followed his four stages, and minor hysteria which did not (Zilboorg 1941). Furthermore, Charcot's psychological insights were greater than most credit him with, he recognised the role of both suggestion and emotions but was uncertain whether they were secondary features. His concern was that as phenomena they were difficult to measure and therefore he

concentrated on neurological signs and symptoms. He was also aware of the narrow boundary between hysteria and malingering:

"the ruse, the sagacity, and the unyielding tenacity that especially the women, who are under the influence of a severe neurosis, display in order to deceive...[particularly to] a physician." (Charcot: trans Sigerson 1877)

Indeed, it was the issue of suggestion and falsification that has resulted in criticism of Charcot by historians. His demonstrations at the Salpêtrière were played out in front of an audience in an emotionally charged atmosphere. It was perhaps not surprising that the hysterical patients developed their symptoms seemingly at will. Some have levied the accusation that there was outright falsification of results, with Charcot's assistants deliberately training patients up in order to please their chief. It is of interest to note that neither Joseph Babinski or Pierre Janet, two of Charcot's most famous assistants, suggest that any such behaviour occurred, although both disagreed with their former master's views on hysteria (Janet: trans Carson 1901, Babinski: trans Cox and Kathol 1988). One cannot help but think that it was the atmosphere of the demonstration alone, perhaps in combination with the obvious financial benefits to poor country girls of remaining a patient that explained the phenomena. Support for the influence of the latter phenomena comes form Axel Munthe's autobiography *The Story of San Michele* (1930). Munthe describes his feelings of frustration about the treatment received by a young country girl from Charcot for hysteria. Munthe considered that her treatment, in

the Salpêtrière, was turning her into a life long invalid, and as such represented a form of imprisonment. He came to her aid and "rescued" her from this, and was disappointed to find that she did not want to return to the country or stay on in his apartment. It transpired that the drama, excitement and rewards of her new hospital life were far more fulfilling than her "normal" existence.

The debate about the veracity of Charcot's demonstrations occurred after his death. During his lifetime a different debate raged. The disagreement centred around Charcot's advocacy of hypnotism. Although originally "prudent and conservative" he developed into a passionate advocate. He declared that those who succumbed to hypnotism could all be induced to have major hysterical paroxysms, therefore hypnosis was a diagnostic test for hysteria. Over time he went further and declared that one could transfer these effects by magnets (Charcot: trans Sigerson 1877). These opinions were passionately disputed by Bernheim his supporters at the Nancy Medical School. Bernheim insisted that the hypnotic state was nothing more than sleep brought about by suggestion. Crucially they demonstrated that succumbing to hypnosis was not the preserve of neuropaths but varied within the population and "the majority of subjects can be readily inclined to it." The debate became increasingly vitriolic over time with Bernheim denying that there was any such thing as a specific disorder hysteria and that Charcot's patients were merely highly suggestible. Charcot responded by describing the Nancy group as unscientific and vague (Veith 1965).

Two other aspects of Charcot's work are of note. His clinical drawing of hysterics were highly similar to artistic depictions of demonical possession from the Dark Ages. This adds further weight to the claims that hysterics were mistaken as being possessed by the devil during the Renaissance (Zilboorg 1941). Secondly, he was frustrated and disappointed at being unable to have his work translated into German. As a result he was exceedingly grateful for an offer of help from a hitherto unnoticed Austrian student. He showed his gratitude by admitting the student, Sigmund Freud, into his inner circle and he did what he could to advance Freud's career (Veith 1965).

It was a testament to Charcot's charisma that many of the great neurologist of the turn of the twentieth century studied under him. From the perspective of the study of medically unexplained symptoms, three students are of particular importance, Pierre Janet, Joseph Babinski and Sigmund Freud. Although it was Freud who was to become the household name and the face of psychiatry to the public, even if latterly not to the profession, both Janet and Babinski's views may be of more current relevance.

Pierre Janet's doctoral thesis was *The Mental State of Hystericals: A study of Mental Stigmata and Mental Accidents* (Janet: trans Carson 1901). In his work Janet echoed Charcot and Briquet's descriptions of episodic and permanent symptoms but it was other features of the thesis that helped develop an understanding of the condition. Janet denied that hysterics were any more erotic than other individuals, and indeed he claimed they were often frigid. The reason for this was due to the shrinking of their emotional

radius, their increasing egocentricity, a preoccupation with their own concerns, and a complete indifference to the demands and expectations of others (Veith 1965). Janet also considered that the *idée fixe* was "below consciousness". It appeared that he welcomed Freudian thinking; "we are happy to see today MM. Breurer and Freud express the same idea" (Janet: quoted Veith 1965). However Janet quickly became less welcoming to the introduction of psychoanalysis and he demonstrated a determination to see his own ideas as being distinct from Freud's. Freud responded with characteristic anger at what he regarded, rather unfairly, as a betrayal:

"Janet behaved ill, showed ignorance of the facts and used ugly arguments. And finally he revealed himself to my eyes and destroyed the value of his own work by declaring that when he had spoken of 'unconscious' mental acts he had meant nothing by the phrase- it had been no more than a *façon de parler."* (Freud: quoted Zilboorg 1941).

The problem really lay in what one meant by unconscious. Janet's tenet was that hysteria was a neurosis that occurred in people who were constitutionally vulnerable due to abnormalities of function in their nervous system as a result of a variety of physical causes,. The unconscious element he commented on was closer in form to automatic thoughts, now described in cognitive-behavioural theories, and as such was potentially accessible to the patient (Janet: trans Carson 1901).

Babinski took a differing view on hysteria and came closer than any of Charcot's other protégés to agreeing with the views of the opposing Nancy school. He was so impressed with the role of suggestion in hysteria that he proposed the disorder be renamed *pithiatism* from the Greek for *peithõ* [I persuade] and *iatos* [curable]. Babinski hypothesis was that hysteria was brought on by suggestion either overt or covert. Of crucial diagnostic importance was the ability to alleviate the symptoms by persuasion, even if the relief was only temporary. He also described emotive hysteria, with a clinical picture which was strongly suggestive of somatic manifestations of anxiety and depression, and reflexive hysteria where tendon and vasomotor reflexes were exaggerated (Babinski: trans Cox and Kathol 1988). This led him to conclude that physicians had a role in the genesis of the illness and that they must guard against making any comment that would engender suggestion of illness within the patient. However, he also realised that there were many pitfalls for the unwary in the diagnosis. His major concern was that conditions secondary to organic lesions, in particular cerebrovascular disorders, were misdiagnosed as hysterical. He also realised that the patient's social situation was important and he was particularly concerned about those who stood to gain through compensation from their symptoms. Within the later context he recognised that symptoms but also signs, such as blisters and ulcers, could be deliberately falsified by patients (Babinski: trans Cox and Kathol 1988). Babinski's theories appear to have been largely unheeded his peers, probably due to the expanding influence of psychoanalysis. Unfortunately, they have also been condemned, unjustly, by historians such as Veith, for their psychological naiveté.

Despite the pre-eminence of many of Charcot's pupils in their own fields only one was to become a household name whose star far outshone his master's. Sigmund Freud revolutionised both psychiatry and Western thought and remains at the beginning of the twenty-first century the only psychiatrist with whom most of the general public are familiar. His theories still have overwhelming influence over all spheres of the Arts, even if his influence on psychiatry has dramatically waned (Findlay 1995). However, whether he ever had any influence over the world of neurology is questionable, many of his contemporary writers rejected his views explicitly (Omerod 1911, Head 1922).

Freud's domination of the first half of the twentieth century has been such that it is difficult to take a neutral stance on what his contribution has been. Much of what he hypothesised had already been described by physicians such as Carter and von Feuchtersleben, on the other hand he undoubtedly brought unity, a dynamic vigour, and a true talent for writing case reports to the field. Freud clearly had the ability to inspire and draw disciples around him, but he was unfortunately unable to accept any dissent, as his dealings with Janet indicate. Indeed, it may be significant that his childhood ambition was to be a great general and his hero was Hannibal (Stafford-Clark1965). The great stumbling block in assessing his work lies on the inability to prove or disprove his views. They fail, and many of his followers explicitly reject, Popper's test of falsifiablity (Popper 1951). Thus Veith (1965) could describe him has having the "final new ideas" which were "beyond challenge" whilst Pelosi (1999) described him as

"Sigmund Freud, the greatest community psychiatric nurse of all time" suggesting that listening and supporting were the mainstay of his treatments rather than the specific merits of analysis.

Freud's evolving interest in hysteria was described in his monograph, co-authored by Josef Breurer, *Studies in Hysteria.*

" but the causal relation between the determining psychical trauma [trauma is taken from the Greek for wound] and the hysterical phenomenon is not of a kind implying that the trauma merely acts as an *agent provocateur* in releasing the symptom, which thereafter leads an independent existence. We must presume rather that the psychical trauma- or more precisely the memory of the trauma- acts like a foreign body which long after its entry must continue to be regarded as an agent that is still at work; and we find the evidence for this in a highly remarkable phenomenon which at the same time lends an important practical interest to our findings.

For we found, to our great surprise at first, that each individual hysterical symptom immediately and permanently disappeared when we had succeeded in bringing clearly to light the memory of the event by which it was provoked and in arousing its accompanying affect, and when the patient had described that event in the greatest possible detail and had put the affect into words. Recollection without affect almost invariably produces no result...." (Freud and Breuer 1895)

In essence, what they were saying was, that which cannot be remembered cannot be emotionally forgotten. However, Freud and Breuer's ideas soon started to diverge. Freud increasingly emphasised sexuality in the aetiology of neuroses whereas Breuer thought it to be of less significance. Although publicly Breuer was supportive, his private reservations irritated Freud.

"Not long ago Breuer made a big speech about me at the Doktorenkollegium, in which he announced his conversion to belief in the sexual aetiology. When I took him on one side to thank him for it, he destroyed my pleasure by saying: 'All the same I don't believe it.' Can you understand that? I can't." (Freud in a letter to Fleiss: quoted Stafford-Clark1965).

Freud went on to distinguish *actual neuroses* from *psychoneuroses*. The *actual neuroses* were disturbances of well-being directly and physically related, via toxic endogenous chemical processes, to the frustration or the excessive discharge of sexual energy. This included conditions such as neurasthenia. *Psychoneuroses*, by contrast, were caused by an unconscious mechanism which converted any disturbance of sexual function into indirect, potentially complex, disruptive yet symbolic physical symptoms. Hysteria was seen as a *psychoneurosis* and separated off from neurasthenia, just at the time when the rest of medicine was heading to the opposite conclusion. In both mechanisms the theory borrows heavily from Galenic spirits and Newtonian mechanics. With the description of

psychoneuroses came a change in the definition of neurosis from its original definition of a organic disorder of function of the nervous system into its current definition implying a disorder mediated by psychological distress alone. It was also responsible for the conceptualisation of hysteria as a conversion disorder.

Freud gradually changed from hypnosis to a purely psychotherapeutic technique, via 'laying on of hands'. It was from this that psychoanalysis developed. There were three central themes, repression, the unconscious and infantile sexuality. It was the development of his theories on infantile sexuality that caused Freud's main problems. Initially, Freud believed that his patients had been subject to sexual assaults in childhood and this led to symptoms in adult life; *the seduction theory*. Then over a three year period Freud began to have doubts and realised that some of his patients were reporting fantasies, with this realisation came the development of his *Oedipal theory*.

"I have found love of the mother and jealousy of the father in my own case too, and now believe it to be a general phenomenon of early childhood....if that is the case, the gripping power of *Oedipus Rex*, in spite of all the rational objections to the inexorable fate that the story presupposes, becomes intelligible...Every member of the audience was once a budding Oedipus in phantasy." (Freud 1948)

Jeffrey Masson launched a bitter attack on this theory in his book *The Assault on Truth* (Masson 1983), in which he argues that Freud was right first time around, and that

Freud's abandoning of the seduction theory was a betrayal of his patients. In fact, both Freud's and Masson's arguments suffer from a commitment to accepting that if an adult reports a childhood memory as having occurred, then the origin of that memory must be in childhood, irrespective of whether the memory was based in fact or fantasy. Neither authors gave much credence to the possibility that the memory may have had its genesis in adulthood and be falsely attributed back to childhood, possibly as a result of suggestion either within or out with the therapeutic setting.

5.7 From shellshock to somatization.

Freud's views on hysteria, although implicitly still accepted, even within the atheoretical Diagnostic and Statistical Manual of Disease, 4th Edition (APA 1994), were significantly challenged by the First World War. The term *shell shock* was first used by Charles Myers to describe three soldiers who suffered from sleeplessness, reduced visual fields and amnesia (Myers 1915). Myers originally intended that the expression would suggest a functional disorder akin to hysteria but in which a physical insult had been a major trigger. However the phrase changed meaning under the influence of Fredrick Mott, who found minute haemorrhages throughout the nervous system of soldiers dying without obvious physical cause. He extrapolated this to suggest that those suffering form shell shock may have had a similar pathology (Mott 1916). Myers remained sceptical:

" I must have been one of the first to use the term 'shell shock' which has since deservedly received adverse criticism. But I was careful to point out the close relations of these cases to those of hysteria and I did not suppose, as Lieutenant- Colonel Fredrick Mott was then attempting to show, that they arose from the effects of minute cerebral haemorrhages or other microscopically visible lesions. I attributed them as they are now generally attributed, to mental 'depression' and 'dissociation', but I was inclined to lay some emphasis on the physical shock produced by the bursting of a shell as a prime cause of the 'dissociation'." (Myers 1940).

As the war progressed and Mott gained experience in the management of 'shell shock he changed his views:

"My opinion regarding the relative importance of the organic factor to the psychogenic in respect of the symptoms of shell shock changed with further knowledge. The psychogenic factor in my judgement is by far the most important cause of the consecutive phenomena." (Mott 1919)

The argument was reminiscent of, and influenced by, one that had been debated over the previous sixty years; could railway accidents cause physical damage to the nervous system that would in turn cause emotional symptoms? *Railway spine* (Erichsen 1866), a pathological emotional state due to putative inflammation of the spine following injury, was a major source of litigation. It was also a major cause of frustration for many, when

litigants spontaneously recovered after settlement of their cases. A well structured argument by Herbert Page (1883) suggested that there was no pathological evidence to back Erichsen's hypothesis of inflammation of the spine, however he did not accept that litigation was causative either. Instead he suggested that the disorder was one of *nervous shock* brought on by fear and as such had a much better prognosis than disorders of the spine. Although he did, somewhat sceptically, suggest that the disorder could be terminated at will thus explaining the spontaneous recoveries following the end of litigation. Initially courts responded by rejecting claims:

"in order to prevent the opening of a wide field.... for imaginary damages....[Mary Coultos was denied compensation for] damages arising from mere sudden terror unaccompanied by any actual physical injury, but occasioning a nervous or mental shock." (Victoria Ry. Comm'rs 1888).

However, opinion swung over the next twenty years as many argued that disallowing such claims was an injustice to those suffering mental illness and particularly traumatic mental disorders (Brown 1990).

A similar issue lay at the heart of shell shock. The First World War demanded absolute patriotism from those involved. Men were conscripted, and humiliated if they failed to fight. Army discipline demanded an established boundary between irresponsible or cowardly behaviour and illness, the distinction between intentional and unintentional

symptoms was of the utmost importance (Myers 1916). Initially shell shock only affected a small number of troops, and undoubtedly some of the 346 British soldiers shot for cowardice were unrecognised sufferers (Babington 1983). This was to change with the Battle of the Somme during 1916. The offensive wiped out almost half a million British soldiers, 'a large part of a generation and much of the best of that generation' (Schmidt and Velder 1984). With the Somme came a vast increase in shell shock cases from 3 000 in the first half of the year to 17 000 by the end of that year (Moore 1974). The fact that sufferers included those of proven bravery and also the sheer scale of the problem meant that it could not be ignored. The War Office recognised the problem and also its effect on morale (Report of the War Office Committee 1922). They were particularly concerned by the 'contagious' nature of the condition, although no-one thought that it was infective in the true sense of the word, it was noted that once soldiers became aware of a case their own risk of suffering increased substantially. 'Epidemics' spread through battalions with disastrous effects, the War Office changed its emphasis from the failings of individual soldiers to the failings of their commanders. Merskey (1979) pointed out that shell shock mirrored other 'epidemics' of hysterical symptoms and putatively suggested that the 'infectivity' was a result of a narrative being supplied via suggestibility through which subjects could react to intolerable distress. In order to contain the problem the army instituted a series of measures. Most importantly soldiers were no longer punished and shell shock was recognised as an illness. The disorder was renamed *Not Yet Diagnosed- Nervous* and a front-line system of triage, treatment and rapid return to combat was

implemented. A gradual acceptance of psychological disturbance came, and both military and civilian audiences became more sympathetic (Merskey 1995).

The sheer scale of the numbers affected by shell shock, and their circumstances, led many to question Freud's concept of a sexual aetiology in hysteria. It seemed improbable, if not impossible, that all these soldiers had sexual neuroses (Merskey 1979). However, the War did serve to emphasise the role of current social circumstances in the development of illness. Thus, whilst it challenged Freud theoretically, the War was responsible for almost total acceptance of the idea that intolerable psychological distress could lead to non-feigned physical symptoms. The influence of the War was so great that the psychological explanations of shell shock became a paradigm for the treatment of neuroses in general, and promoted the influence of psychoanalysis (Riggs 1922). This interpretation of the war's influence on psychoanalysis has been challenged as a 'whiggish' interpretation by some authors (Wessley 2000). Whilst it clearly had such an influence on psychoanalytic culture it is less clear that society as a whole shared this interpretation.

Psychoanalysis itself, did not stop with the ideas of Freud and several other analysts made influential contributions to the understanding of unexplained symptoms. Wilhelm Steckl, a close confederate of Freud and a founding member of the Wednesday Society in Vienna, was generally credited with introducing the word *somatisation*. Steckl disagreed with Freud over the theory of *actual neuroses*, and held that all neuroses were

psychic neuroses. Whilst Freud had been reluctant to attribute predominantly physical conditions to psychic events, Steckl had no such qualms. He considered that many cases which were diagnosed by physicians as heart-trouble, asthma or stomach complaints were in fact due to psychic problems. The fault lay with physicians who had not understood "the organic language of the soul" (Steckl 1923). However, examination of Steckl's cases (Steckl 1953) demonstrates examples of putative, and perhaps somewhat unlikely, conversion hysteria characterised by marked symbolism. Examples included a man with a swollen knee, which Steckl believed was, symbolic of the swollen head of his father who had died after a fall. Steckl's somatisation was really an all inclusive theory of conversion hysteria and bears little resemblance to the modern DSM IV concept of somatization disorder (APA 1984).

Steckl went on to explain that there were specific areas of predilection for organic responses to psychic conflicts (Berrios and Mumford 1995). This idea was pursued by Franz Alexander at the Chicago Institute for psychoanalysis, who hypothesised that rather than specific areas, there were specific disease states that were psychosomatically determined. These were typified by hypertension, neurodermatitis, asthma, rheumatoid arthritis, duodenal ulcers, ulcerative colitis and hyperthyroidism (Alexander and French 1948). Alexander went on to suggest that there were two aetiologies to somatic symptom formation, *conversion* and *vegetative*. As already described conversion symptoms allowed relief of emotional tension by allowing symbolic expression. Vegetative neurosis by contrast was manifested through direct physiological actions,

secondary to emotions caused by chronically established, and therefore unresolved, conflicts.

Although the history of psychoanalysis was littered with schisms and factions right from its very beginnings, Ronald Fairbairn was probably the first influential analyst to move completely away from Freud's ideas of impulse-psychology and ego psychology. Fairbairn viewed the concepts of hysteria as being discovered by Janet with his description of *dissociation* (Fairbairn 1944). Fairbairn modified Janet's theories in line with his own theories of *object-relations* psychology.

"Hysterical conversion is of course a defensive technique- one designed to prevent the conscious emergence of emotional conflicts involving object-relationships. Its essential and distinctive feature is the *substitution of a bodily state for a personal problem;* and this substitution enables the personal problem as such to be ignored. All personal problems are basically problems involving personal relationships with significant objects; and the objects involved in the conflicts of the hysteric are essentially *internal objects*- and more specifically the exciting and frustrating objects [italics, Fairbairn]" (Fairbairn 1954).

Over the next twenty years the various psychoanalytic schools modified these basic theories in an attempt to describe the underlying psychopathology of hysteria. Whilst there may have been important insights contained within their writings the overall effect

appears to have been a broadening of the concept of hysteria to stage were it meant all things and nothing. Of particular concern was that theories of hysterical personality were now allowing for all those displaying such traits to labeled hysterical, irrespective of the presence of medically unexplained symptoms.

5.8 The rise of the social model.

It would be wrong to think that the first half of the twentieth century was dominated solely by psychoanalysts. The discipline of sociology was also to make some important theoretical inroads, and which, reviewed retrospectively, have stood the test of time better. Foremost among them is Talcott Parsons' *The Social System.* (Parsons 1951). Parsons, although not rejecting emipiricism, was an unapologetic theorist. He was clearly influenced, to some extent, by his psychology contemporaries but he thought that individual dynamic insights were of little value if viewed out-with the context of the structures in which they were made. Parsons changed the definition of "being sick" from one related to "a condition" to one of a "prescribed role". As Parsons' saw it the "test is the existence of a set of instituitionalized expectations and the corresponding sentiments and sanctions" (Parsons 1951).

There were four aspects to the institutionalized expectation system relative to the *sick role*. First, the sick individual was exempt from their normal social responsibilities to a nature and extent relative to the degree of illness severity. This required legitimization and that came from a physician, who was thus placed in the role of arbiter. This was

clearly a protection against 'malingering' at a societal level. Second, the sick person could not be expected to get better simply by "pulling himself together", it was critical that the illness was due to "a condition" not an "attitude". Third, the sick person had to want to get better and fourth they had an obligation to seek "technically competent" help (Parsons 1951). Parsons argued that the sick role thus defined became the object of significant *secondary gain*, which the patient could be unconsciously motivated to secure. It can be seen that patients with unexplained symptoms could cut across all the institutionalized boundaries of the *sick role* failing the test of legitimization as their symptoms could not be defined, nor accurately separated from malingering, except on a basis of trust. Furthermore, as has been demonstrated, there had, over the last 300 years, been an increasing view that their symptoms were related to an attitude and that pulling themselves together should indeed be possible. The sick role outlined why those with unexplained symptoms may have wanted to become "ill" and offered an explanation of the subjective overwhelming need for a legitimising diagnosis, as well as explaining a punitive element towards such patients.

It also offers an interesting insight into doctors' responses to those who don't fit into the pre-prescribed roles. In discussing unnecessary surgery Parsons quotes the ideas of the Malinowski:

" a pseudo-scientific element in the technical competence of the medical profession which is more than simply an expression of the relative lack scientific development of

the field; it is positively motivated.....cluster about situations where there is an important uncertainty factor and where there are strong emotional interests in the success of the action...[such as]....gardening and deep sea fishing...[this form of] pseudo-science is the functional equivalent of magic in the modern medical field....it is to bolster the self-confidence of actors [surgeons] in situations were energy and skill *do* make a difference but because of uncertainty factors, outcome cannot be guaranteed. [This suits both participants, i.e. doctor and patient; italics Parsons]" (Parsons 1951).

Further sociological understanding of illness came from the work of David Mechanic. Mechanic had been stimulated by the work of Koos (1954) *The health of Regionsville*. Koos described the views on health of 500 families in a small American town. He made the striking discovery that people experienced many more symptoms than they presented to doctors with. That may seem rather obvious, but at the time it represented a radical challenge to the patho-anatomical medicine of the nineteenth and early twentieth century (Armstrong 1986). Mechanic attempted to explain this phenomena in terms of *illness behaviour* which he defined as "the way in which given symptoms may be differentially perceived, evaluated and acted upon (or not acted upon) by different kinds of person" (Mechanic 1962). Illness behaviour could therefore be influenced by cultural, social or sex-role expectations or may be subject to variation as a result of previous illness experiences, situational factors or adaptive needs. The key factor was that different people would react differently to the same pathology, as a result of a diverse array of psychological and social variables (Mechanic 1977). It also offered a

patient centered view, and as such one that was directly applicable, rather than the societal level view of the *sick role* which necessitated the reactions of others. Although the theory was predominantly centered around pathological disease processes it still influenced a significant shift from analytic thinking as it allowed, and validated, the patient's thoughts and previous experience rather than consigning them to unconscious sources of trauma.

Pilowsky (1969) recognised that although Mechanic's theory was intended to be universal his main concern was, in reality, the under-reporting of symptoms. Pilowsky, through his interest in unexplained symptoms, was by contrast more concerned with those who over reported symptoms. Borrowing from Mechanic he felt such patients may be best described as having *Abnormal Illness Behaviour*. Implicit within this definition lay the idea that unexplained symptoms could have a heterogeneous aetiology. Pilowsky, himself, recommended physicians inquire into the nature of the somatic component of the patients symptoms, but also their ideation and affect, their attitude to others, their motivations and any relevant cultural factors in order to understand the presentation. One potentially useful, but scientifically difficult, aspect of this concept was that it allowed for coexistence of both unexplained symptoms and pathological disease. Armstrong (1986) criticises all three of these models for assuming that the doctor is at the rational centre and it is with the patient that the "problem" lies.

"Put simply it is not the illness which brings the patient to see the doctor but the theory....Abnormal illness behaviour was invented to cope with a problem, namely symptoms without disease, which was medically incomprehensible. But is it patient behaviour which is 'abnormal', 'maladaptive', or just plain wrong, or is it medical theory itself which cannot adequately account for the phenomena it observes? Why is it that doctors react with such strong emotion, 'hostility', or feeling hunted, to patients with symptoms but without an organic lesion? Is it not the doctor's response which is abnormal." (Armstrong 1986).

5.9 Operationalization and Obituaries

The ever expanding definition of hysteria and loosening of the central concept of tying hysteria to the presence of unexplained symptoms led to an inevitable backlash during the 1960's. Three works were of particular significance, *The Myth of Mental Illness* by Thomas Szasz (1961), the operationalization of Briquet's syndrome by Guze *et al* (1962) and *Diagnosis of Hysteria* by Elliot Slater (1965).

Szasz influence has now all but completely waned, but Guze and Slater remain influential. Guze's operationalization of a psychiatric disorder formed the basis of the modern classification systems such as the Diagnostic and Statistical Manual of Disease (APA) and Slater's paper remains the one which most British physicians and psychiatrists recall first when discussing unexplained symptoms. However, in its day, *The Myth of Mental Illness; A critical assessment of the Freudian approach* was

essential reading to anyone in the field of mental health. Szasz's critique dealt almost exclusively with hysteria. He argued that as it was the first *functional* illness to be described it merited closest examination, but others, such as schizophrenia, would follow the same rules. It was this assumption that really undermined Szasz's argument. Historically, as has been demonstrated, the insanities had never really been considered similar to hysteria and it was only was only under the umbrella of psychoanalysis that any links had been seriously made. Furthermore, experiments, conducted within Szasz lifetime (Johnstone *et al* 1976), had demonstrated an organic basis for psychotic illness. Szasz refused to concede the importance of this and made his position untenable.

These criticisms aside, Book 1 of the *Myth of Mental Illness* does offer a well constructed critique of, the then contemporary zeitgeist, analysis; and finds it wanting. Szasz hypothesised that the problem began with Charcot who, when faced with a group of patients who may or may not be malingering, gave his clinical, and by implication, moral authority to describing them as sick and thus legitimizing them. This being done attention then turned to malingering itself, which under analytic thought, demonstrated a psychological need. Therefore all malingerers were psychiatrically unwell and by extension all suffering, irrespective of whether it was hysteria or malingering, was illness. The problem then arises that such disorders have less prestige than a "physical" disorder and it is therefore desirable for psychiatrists and analysts to turn away from their supposed psychological insights and claim that they too are, ultimately, searching for a putative physical mechanism. Thus any sign of distress is an organically based

physical *illness* and the concept thus becomes serendipitous, and too over inclusive to be meaningful.

Another alternative to the psychoanalytic approach was introduced by the St Louis group in the United States. They were concerned with the need to develop widely accepted, valid, diagnostic criteria for psychiatric disorders. Their contribution was to attempt to operationalise the diagnosis of hysteria, on the basis of psychopathology, but validate it against outcome and family data. They started using criteria based upon Paul Briquet's treatise of some 100 years earlier. To make the diagnosis, a lifetime history of, at least 25 unexplained symptoms from 9 groups were required. Further, disease onset should be before the age of 35 (Guze *et al* 1972). They were able to demonstrate the diagnostic stability and validity of the syndrome and also show familial clustering (Guze *et al* 1986). The only criticism of their approach is that they used cases at such a severe end of the spectrum that their results only applied to a small proportion of MUS patients. Nonetheless, the approach still holds influence today and can be seen in both the DSM (APA 1994) and ICD (1992) classifications of psychiatric disease. It is particularly notable that, in the absence of defined aetiology, their classification was atheoretical.

The historical overview of the ideas that have driven research and understanding on unexplained symptoms closes with Elliot Slater's critique on the *Diagnosis of Hysteria,* which must be evaluated in light of the contemporary concern at the overuse, and wildly

differing use, of the diagnosis. Slater opens his critique by quoting Lord Brain's distinction between *adjectival* and *substantival* views of hysteria:

" If hysteria is regarded as a disease...it tends to encourage the belief that it is necessary to decide whether a patient is suffering from hysteria or from something else. But if the patient is regarded as a hysteric it allows for the possibility that he may have other things the matter with him as well. He may be reacting hysterically to mental subnormality or depression, or even...to anxiety. He may have hysteria and epilepsy, or hysteria and some organic brain disease. On the other hand, the substantival idea of hysteria as a disorder leads to the inquiry as to what abnormality hysterics have in common which leads them to react characteristically. This can be expressed in psychological terms, or...in terms of disordered neurophysiology. The two modes of explanation, of course, are complimentary and not mutually exclusive." (Brain: quoted Slater 1965).

Slater offers qualified acceptance of the adjectival form but emphatically rejects the substantival form:

"All the signs of "hysteria" are the signs not of disease but of health. The patient who cannot speak can phonate; it can be shown that the anaesthetic patient does feel; the patient with hysterical amnesia can be brought to recall. "Hysteria", one might say, is not an illness, but health, even if from the doctor's point of view it is in the wrong

place. One cannot build up a picture of an illness out of elements which are severally the evidence of absence of illness. No unitary concept is to be reached this way." (Slater 1965).

Slater goes on to describe a cross sectional study of 112 patients identified by retrospective case note sampling of with "hysteria" at the National Hospital for Nervous Diseases, Queens Square. Slater managed to contact 85 (76%) of them and was alarmed at his findings. In the time since initial diagnosis, an average of nine years, eight patients had died of organic disease which must have been present at the time of diagnosis, four had committed suicide, 19 had had the diagnosis of hysteria as an accompaniment to an organic condition, and in 22 cases the patients had subsequently developed an organic condition which had been undetected at time of initial diagnosis of "hysteria". In total, 49 (58%) of patients in whom "hysteria" had been diagnosed had an underlying organic illness. Perhaps not surprisingly his conclusions were damning:

"What, then, is our conclusion? Looking back over the long history of "hysteria" we see that the null hypothesis has never been disproved. No evidence has yet been offered that the patients diagnosed as suffering from "hysteria" are in medically significant terms anything more than a random selection. Attempts at rehabilitation of the syndrome, such as those by Carter and by Guze, lead to mutually irreconcilable formulations, each of them determined by their terms of reference. The only thing that "hysterical" patients can be shown to have in common is that they are all patients. The malady of the

wandering womb began as a myth, and as a myth it yet survives. But, like all unwarranted beliefs which still attract credence, it is dangerous. The diagnosis of hysteria is a disguise for ignorance and a fertile source of clinical error. It is in fact not only a delusion but also a snare." (Slater 1965).

Slater's obituary was not universally welcomed. In a reply, Sir Francis Walshe (1965) was extremely critical of Slater both intellectually and clinically. He reminded Slater that misdiagnosis and validity were not the same concept and also delivered a warning, when he reminded him that it is physicians who see such patients, and psychiatrists would do well to respect their clinical skills. Sir Aubrey Lewis (1975) commented that hardy words like hysteria tend to outlive their obiturists. He appears to be correct

5.10 Conclusions

This review demonstrates that a clear link can be drawn between the concept of hysteria in the ancient world and the modern concept of medically unexplained symptoms. Furthermore, the review demonstrates that such symptoms have existed in all cultures throughout history.

However the way in which MUS have been viewed through their history has changed dramatically. Although the influence of Aristotle and Plato's concepts of the mind/psyche can be seen to have held influence over Galen, Descartes and many others into the present day, it was with the seventeenth century association of hysteria and the

mind that the stigmatisation of the condition appears to have begun. Throughout history it has been unacceptable for the mind to be viewed as sick. Perhaps nowadays few patients view it as an offence against God but similar stigma still exists. At times, such stigmatisation has seemed deserved and the possibilities of malingering for personal gain have existed. However this view can be tempered with the realisation that at other points people have been tortured and killed for the same symptoms. Whilst there can be little doubt that social factors influence the presentation, the mechanism appears to be more complex than simple falsification.

Warnings too are sounded by this historical review. It can be seen that time and time again the psychologists argued with the somaticists for complete explanations. Yet to date, no one theory has accounted for these conditions. It is particularly depressing to see an almost identical rerun of the nineteenth century neurasthenia debate being repeated at the end of the twentieth century over chronic fatigue syndrome with none of the lessons of history being lent.

This author is left with the feeling that as a patient he would wish to consult a doctor such a Sydenham. A physician who recognised the patients complaints and suffering as genuine but realised that disease did not occur in a vacuum and that the patient's mental state, personality, fears and social situation were all of importance. Physical remedies were prescribed along with supportive psychotherapy, active rehabilitation and changes

to lifestyle in order to help those suffering from a condition that has indeed been shown to be a true test of a doctor's sagacity.

Chapter 6. Medically unexplained symptoms: a narrative review of the literature.

6.1 Introduction.

This narrative review of the literature on medically unexplained symptoms will aim to provide an overview of the field in order that the systematic review of medically unexplained symptoms in neurology may be placed in a context. It will begin by outlining epidemiological data from studies based in community, primary care and secondary care settings. There will then be a discussion of the relationship between MUS and depressive symptoms, the effect of depression on disability and the effect of depression on the outcome of physical disease. The third section will describe some of the major aetiological theories in MUS with reference to biological, psychological and social theories. Some of the major theories, particularly sociological ones, were described in chapter 5 and they will not be repeated. The review will close with a discussion on the detection, management and treatment of MUS.

6.2 Epidemiological studies.

The Epidemiological Catchment Area programme (ECA; Reiger 1984, Eaton 1984) has been one of the major sources of data on the community prevalence of psychiatric and related disorders. This United States study used a multi-stage, random and clustered sampling technique to provide a large, epidemiologically sound sample, who were then examined using the Diagnostic Interview Schedule (DIS; Robins 1981). The data on 13 538 of these subjects was examined by

Kroenke and Price (1993) in order to estimate the prevalence of MUS in the community. They demonstrated rates of between 6% and 36% for individual symptoms (table 6.1). To register, a symptom had to be persistent and troublesome, not just a one-off episode. Women were more frequently troubled than men across the range of symptoms with the exception of chest pain. The presence of any physical symptom was associated with a two-fold increase in the rate of psychiatric disorder. Some symptoms, such as insomnia and fatigue were closely associated with depressive disorders. Other symptoms such as dizziness, chest pain and bloating were particularly associated with somatoform disorders. The major flaw with this study was that the diagnosis of MUS was made from DIS symptom profiles and patients' self-report information, rather than a physician-led diagnosis.

Escobar *et al* (1987) reported on the Los Angeles sub-sample of the same data set. They were concerned that the DSM III category of somatization disorder, which required a minimum of 12 unexplained symptoms, was overly restrictive. Indeed, earlier ECA reports had found this definition to apply to only 0.1% of subjects (Robins 1984). They created criteria, derived from results of the DIS interview, and defined somatizing as four or more unexplained symptoms in men and six or more in women. This gave a community prevalence of 4.4%. They too found that chest pain, palpitations and bloating, as well as, gynaecological problems and head and back pain were particularly associated with somatoform disorders. They also noted an increased rate of depressive disorders in their somatizing patients.

Table 6.1. **Community prevalence rates of individual physical symptoms.**

Symptom	Adjusted community prevalence
Joint pain	36.7
Back pain	31.5
Painful menses	30.4
Irregular menses	28.4
Headache	24.9
Chest pain	24.6
Limb pain	24.3
Heavy menses	23.9
Abdominal pain	23.6
Fatigue	23.6
Dizziness	23.2
Insomnia	19.2
Dysuria	19.2
Trouble walking	18.3
Palpitations	18.2
Gas or bloating	17.8
Vision blurred	16.7
Constipation	14.3
Dyspnea	13.8
Nausea	13.7
Missed menses	13.7
Diarrhea	12.4
Fainting	11.7
Weakness	11.3
Loss of feeling	8.4
Vomiting	6

1- from Kroenke and Price (1993)

In primary care settings the largest epidemiological study of unexplained symptoms was undertaken by the World Health Organization (WHO; Gureje *et al* 1997). This study had a two stage sampling technique. First subjects presenting to primary care were screened using the General Health Questionnaire- 12 item (GHQ; Goldberg 1988), then there was a stratified selection according to GHQ score. An emphasis was placed on high scorers and 96% of potential subjects participated. In stage 2, subjects were examined for physical illness, psychopathology (Composite International Diagnostic Interview; Wittchen 1990) and disability (Social Disability Schedule; Wiersma 1990). A total of 5 438 subjects (response rate 62%) from 15 centres were assessed. They found that somatization disorder (SD) as defined in ICD 10 (WHO 1992) was relatively infrequent, with a prevalence of 2.8% (95% CI 2.4% to 3.2%). The rate of DSM III-R somatization disorder was even lower at 0.9%. When the less restrictive definitions suggested by Escobar *et al*, renamed Somatic Symptom Index (SSI), were used they found a prevalence of 19.7% (18.7% to 20.8%). The prevalence rates were similar in 10 of the 15 centres. The major exceptions were the two South American centres where markedly higher rates of both SD and SSI were found. They also found that somatizing patients were a mean of 3 years older than other clinic attenders (42.6 opposed to 39.1) and that females subjects had an increased rate of SD in all centres except Santiago. However when the less restrictive SSI definition was used the sex difference was unremarkable. An unexpected finding was a mild protective effect of formal education. Similar to community studies SSI was strongly associated with both depression and anxiety disorders. Across all cultures SSI was linked to increased social and occupational

disability. Patients with SSI had over twice the number of days off work or not fulfilling their usual roles in the previous month compared to other clinic attenders.

The data from the WHO study is particularly useful as, unlike the ECA, they also studied outcome. Of those patients who met criteria for SSI 67% were successfully re-examined 12 months later. Of those patients, 48.7% still met criteria for SSI. Additionally they were also able to calculate an incidence rate of 7.1% (6.1% to 8.3%) for new cases of SSI. Unfortunately the attrition rate from this study was considerable with one third of eligible patients being lost at initial recruitment and a further third being lost to follow up. Nonetheless the data set was large and indicates that in at least a substantial minority of patients MUS persists. Joint pain, back pain and headache were noted to have particularly poor outcomes. Other factors associated with poor prognosis were older age and longer symptom duration. Logistic regression modelling also suggested that poor self evaluation of health and impaired work roles were predictive of a poorer outcome.

Other studies in primary care have shown similar prevalence figures in various countries: Denmark (Fink 1999), Canada (Kirkmayer 1993), Spain (Lobo 1996) and the United Kingdom (Bridges 1985).

Studies conducted in secondary care settings have shown similar findings (Hamilton *et al* 1996, Nimnuan *et al* 2000). Of most interest are two papers from Leiden, Netherlands. Van Hemert *et al* (1993) found that in a consecutive series

of 191 general medical out-patients, 100 had MUS. This paper was methodologically interesting. First, there was a physician-led diagnosis informed by physical examination and investigations where necessary. Such rigour was lacking in primary care studies and absent in community ones. Second, the diagnosis of MUS was made on the basis of the presenting symptom and not upon the criteria of reaching a certain number of symptoms. Indeed only one fifth of the patients with MUS described in this study reached criteria for DSM-III-R somatoform disorder (similar to SSI). Thirty six percent of the patients with MUS also met Present State Exam (Wing 1974) criteria for a psychiatric disorder, the majority having depression. Speckens *et al* (1996) reported on the outcome of 81 of these 100 patients with MUS. They found a high rate of spontaneous remission. At 15 months follow up 30% had recovered and a further 46% had improved. Female sex and a higher number of unexplained symptoms predicted a poorer prognosis. The less restrictive definition resulted in a report of a more favourable outcome for MUS. Additionally, the report was potentially more related to everyday clinical practice and allows a prognostic estimate on all patients to be made rather than just the few who fulfil arbitrary criteria.

However, not all studies in secondary care suggest such favourable outcomes for MUS. Potts and Bass (1995) reported on the 10 year outcome of patients with chest pain and normal coronary arteries. They found that 74% of patients were still symptomatic at follow up examination. Functional capacity was markedly reduced in this group of patients and one third were unfit for work. Only a fifth of patients had not had a depressive or anxiety disorder during the follow up period.

Panic disorder was common, as a result of chest pain being the index symptom, but less easy to explain was the high frequency of simple phobias which also been noted in other studies of non-cardiac chest pain (Katon *et al* 1988, Beitman *et al* 1989).

From a British perspective it is also desirable to discuss the South London Somatisation study (Craig 1993). Although thoughtfully designed there are both theoretical and practical concerns about this study. Theoretically, an explicit assumption was made, *a priori*, that somatisation represented the somatic presentation of depressive or anxiety disorders. Although this is perfectly acceptable it allows for little comparison with either ICD or DSM definitions of somatoform disorders which concentrate on the number of medically unexplained symptoms a patient has. Indeed, DSM specifically excludes physical symptoms that are better explained by a mood disorder. Practically, there are concerns that the study was only able to identify 44 'somatisers' out of a population of 1135 subjects presenting to primary care, a far lower prevalence rate than was found in any other comparable sample. This study in line with the WHO study found that approximately half of patients with somatoform disorders remitted during the follow up period. They also noted that mood disorders tended to precede somatoform disorders and that remission of the mood disorder was associated with remission of the unexplained symptoms. Interpretation of this finding is difficult as entrance criteria for the study demanded a mood disorder for inclusion. Thus patients who had somatic symptoms but no mood disorder were excluded but may have shown a different pattern of onset.

Additionally, they noted an association between childhood illness experiences, lack of parental care and adult somatisation. They also attempted to study the hypothesis of *secondary gain*, which they defined as the development of physical illness to reverse or prevent the undesirable consequences of a crisis. On the basis of their results they suggest that 'somatisers' were more likely to respond to external events in this fashion. By contrast 'psychologisers' were more likely to respond with neurtalising strategies. It must be remembered that observations of associations do not demonstrate a direction of effect.

An examination of the health of servicemen who served in the Gulf War may seem an odd choice for the final epidemiological study to be cited in this review, but the results are of considerable interest to the study of unexplained symptoms. From late 1990, the UK deployed 53 462 military personnel to the Persian Gulf War. In the months after the war anecdotal reports of various illnesses affecting veterans gradually emerged. The Gulf War Illness Research Unit at Guy's, King's and Thomas's in London conducted a study to compare the health profiles of those who served in the Gulf with those who served in Bosnian conflict and an era cohort of servicemen who were on active duty at the time of the Gulf War but were not deployed. They found that Gulf War veterans reported more symptoms than the two comparison groups, but unlike civilians with multiple symptoms their associated disability was low. There was no evidence of an excess of birth defects, cancer or death (Unwin 1999). This finding held when all confounding factors, including psychological distress, were controlled for. When the symptom patterns were explored using a factor analytic technique there was no difference between

the symptom patterns reported by the three groups, the Gulf War veterans just reported more (Ismail 1999). In an attempt to explain this, the group examined possible exposures to a large list of pathogens, both physical and psychological. They noted an increased exposure, among the Gulf cohort, to smoke from burning oil wells, multiple vaccinations against biological warfare, and measures to protect against, as well as possible exposure to, chemical warfare. It has been suggested that multiple vaccinations can produce a shift in the cytokine profile from Th1 to Th2 (Rook 1997), this altering of the immunological response to vaccination offers a potential biological explanation for the increased rate of symptomatology. Equally, although it is uncertain whether there was any real exposure to chemical warfare in the Gulf, there is no doubt that the threat was real. Almost all veterans examined remember wearing nuclear-biological-chemical protection suits under the desert sun. The group's conclusions were that although there was no evidence of a specific Gulf War Syndrome, being in the Gulf was associated with more deterioration in health than being present in other combat zones. They suspect the mechanisms linking the unique nature of exposures in the Gulf to ill health may be non-specific and related to perceived threat, but acknowledge the possibility that there may be a unique biological mechanism via vaccinations.

6.3. Physical symptoms, depression and health status.

Simon *et al* (1999) re-examined the WHO data set, described previously, to explore the relationship between MUS and depression. They assessed the relative merits of three definitions of 'somatization'. First, the Goldberg and Bridges

(1988) definition where patients with anxiety or depressive disorders present with somatic symptoms. Second, the Barsky definition of somatosensory amplification (Barsky 1992) which emphasises the role of psychological distress in modifying the perception and reporting of somatic symptoms. Third, the denial of psychological distress via the substitution of somatic symptoms as a psychological defence mechanism (Kleinman 1977). Their most robust finding was that the symptomatic experience of depression varied little between cultures and that it was integrally linked with the experience of physical symptoms. They found little evidence to support the concept of somatization as a defence mechanism but did find evidence supporting the other two definitions. The methodology of this study is open to challenge as the group started by defining cases of depression within the data set, this in essence assumes the Goldberg and Bridges definition rather than the Barsky one. The latter would require the unit of study to be symptoms not mood.

The reverse perspective was in fact examined by Katon *et al* (1990). They identified a cohort of 'high utilizers' of primary care services then examined them for unexplained symptoms, depression and disability. Their results suggest that MUS lie on a continuum where increasing levels are indicative of increasing distress, disability and maladaptive illness behaviour.

Hotopf *et al* (1998) exploited a large data set from the Medical Research Council's Survey of Health and Development (Wadsworth 1992) to examine the same question. They found a similar distribution of physical symptoms to the one

found in the ECA, but they had the advantage of data from repeat assessments seven years apart. This allowed them to show that psychiatric disorder was associated with a 2.9- 6.9 increase in the odds of developing a physical symptom. Conversely, each physical symptom increased the risk of a psychiatric disorder. Both these factors were associated with disability in a dose-response relationship. Logistic regression analysis found that both factors acted independently, at least to some extent, in causing disability. They then created a model where it was artificially assumed that the presence of a psychiatric disorder 'caused' any detected physical symptoms. Even with this assumption, psychiatric disorders only accounted for 40% of physical symptoms. It should be noted that the interpretation of this study hinges on the assumption that in a community sample of 36 year olds few physical symptoms will be explained by organic disease.

The role of depression in the causation of disability, irrespective of the presence of MUS, has been a topic of increasing interest over the last ten years. In a seminal paper Wells *et al* (1989) measured the functioning and well being of patients with major depressive disorder and compared them to patients with other chronic medical conditions. The comparison groups included diabetes, advanced coronary artery disease, angina, arthritis, gastro-intestinal disease, respiratory disease and back problems. Depressed patients had functioning which was significantly worse across a range of domains. The only group with comparable disability were the advanced coronary artery disease patients (ACAD). Furthermore the disability effects were additive, thus ACAD plus depression was associated with roughly twice the reduction in social functioning than either group

alone. In a separate study Judd *et al* (2000) demonstrated chronic and pervasive disability as a result of uncomplicated major depressive disorder in a ten year follow up study of 371 patients. They also found that the disability disappeared when patients became asymptomatic indicating that it was a state dependent phenomena not a trait.

The presence of depression and co-morbid physical disease not only leads to poorer functioning but also poorer outcome, even for so called 'hard measures' such as mortality. In a well conducted, community-based follow up study, Schulz *et al* (2000) found that depression was an independent risk factor for mortality with a relative risk of 1.24 (95% CI 1.06 to 1.46). This compared to the increased risks of 1.26 (1.08 to 1.47) for hypertension and 1.96 (95% CI 1.55 to 2,47) for current congestive cardiac failure. In a specific examination of post-myocardial infarction patients the presence of major depressive disorder was associated with a four-fold increase in mortality even when the severity of coronary artery disease was strictly controlled for (Frasure- Smith *et al* 1993, Lesperance *et al* 1996). Similarly, Sullivan *et al* (1997) reported that the presence of depression at the time of diagnosis of coronary artery disease by angiogram was more predictive of functional status 1 year after diagnosis than the number of coronary arteries occlude by more than 70%. Similar findings have been reported in stroke research (Parikh *et al* 1992 and inflammatory bowel disease (Walker *et al* 1996).

6.4. Aetiological theories.

Whilst the epidemiological literature is relatively well embedded in the general field of MUS and somatization, the same cannot be said for the aetiological literature. Much of it is diversely situated and little of it is definitive. The majority of the emphasis on biological theories concentrates on 'end-organs' an is embedded in the literature on specific syndromes e.g. chronic fatigue or irritable bowel. Additionally there are two fields, pain and hypochondriasis, which are highly relevant but have developed their own literature with little overlap with MUS.

Biological hypotheses

Genetics:

To date most genetic studies have concerned themselves with familial aggregation. Early studies concentrated on hysteria, although exactly what the term meant varied between studies. Ljungberg (1957) studied families of 381 Swedish probands with conversion disorder and found increased rates of conversion disorder in both male and female relatives. Slater (1961) conducted a twin study of 12 monozygotic and 12 dizygotic twin pairs. He failed to find any hysteria in the co-twins. It should be noted that, like his outcome study, he lacked any satisfactory definition for the unit of study. In a series of papers by the St Louis group on hysteria, somatization disorder, they suggested a heritable component following the discovery of increased rates among the female relatives of index cases (Arkonac and Guze 1963). In addition they suggested that there was a genetic association with alcoholism and psychopathic personality disorder

in male relatives (Guze *et al* 1971, Cloninger *et al* 1975, Cloninger *et al* 1986). In more recent work which examined hysterical paraplegics who had had previous functional illnesses led the authors to conclude that predisposing personality factors could be the mechanism for a genetic influence on presentation (Baker and Silver 1987).

More recent, prospective, work has shown familial clustering in fibromyalgia (Hudson *et al* 1992, Stormorken and Brosstad 1992, Pellegrino *et al* 1989) and that family members also have higher than expected rates of irritable bowel syndrome, migraine headaches, and mood disorders (Hudson *et al* 1992, Messinger *et al* 1991).

In a well conducted twin registry study of MUS, Kendler et al (1995) found that genetic factors accounted for 25-50% of the total variance in reported symptoms, whereas familial environment accounted for virtually no variance at all.

However, despite these suggestions of a genetic factor in the aetiology of MUS one must surmise that no conclusive evidence of genetic transmission has been demonstrated (Boham *et al* 1984).

Triggering events:

Triggering events have been well described in MUS syndromes. Fibromyalgia can be triggered by physical trauma such as a motor accident (Waylonis and Perkins 1994), CFS by viral infections (Goldenberg 1989) and most MUS syndromes by

emotional stressors (Culclasure *et al* 1993, Hazlett and Haines 1992, Dailey *et al* 1990).

Neurophysiology:

Prasher *et al* (1990) examined neurophysiological markers in chronic fatigue patients using evoked potentials. They found normal somatosensory, auditory and visual evoked potentials, but noted that there were abnormalities in the long latency potentials, particularly P300, in about half the cases. However, such findings have also been demonstrated in schizophrenia (Blackwood *et al* 1999) and more recently in major depression where sleep disturbance was a marked feature (Bruder *et al* 1991). Attempts at replication have not been completely successful although abnormalities have been found in auditory tasks but not visual ones (Scheffers *et al* 1992).

Neuroimaging:

The majority of neuroimaging studies have been conducted in the chronic fatigue research. Interest in the possibility of structural abnormalities in the brains of fatigue patients arose following a report on the 'Lake Tahoe' epidemic where magnetic resonance imaging abnormalities (MRI) were found in 78% of subjects (Buchwald *et al* 1992). However, it is unclear who and what was actually studied as many patients had seizures, psychosis and dementia (Holmes *et al* 1987). Local doctors later reported that many of the subjects were not from the Tahoe area at all but had come to the area to have their symptoms investigated in response to media interest (Boly 1987). More recent studies using MRI in chronic fatigue

have failed to demonstrate any increase in abnormalities (Cope *et al* 1995, Greco *et al* 1997). It has been noted that the potential for confounding with depressive disorders exists particularly in examinations of white matter hyperintensities (Buchwald *et al* 1992, Dupont *et al* 1990, Brown *et al* 1992).

As few currently postulate the possibility of macroscopic brain lesions in CFS interest has turned to functional brain imaging (Wessley *et al* 1998). To date most functional studies have used Single Photon Emission Tomography (SPET) but the methodologies used have suffered from a lack of standardised techniques for reporting abnormalities in cerebral perfusion. The results have been mixed with reports of global hypoperfusion (Ichise *et al* 1992, Schwartz *et al* 1994), localised hypoperfusion (Costa *et al* 1995, Goldstein *et al* 1995) and no significant differences between subjects and healthy controls (Peterson *et al* 1994) or depressed controls (Fischler *et al* 1996). MacHale *et al* (2000) attempted to overcome some of these methodological problems and found that both patients with chronic fatigue and depression had increased perfusion in the right thalamus, pallidum and putamen compared to healthy controls. However, there was differences noted in perfusion of the left thalamus and left prefrontal cortex between fatigue and depressed patients. This should be interpreted in view of the fact that different results were found depending on whether a 'region of interest' (Ebmeier *et al* 1991) or statistical parametric mapping (Friston *et al* 1995)analysis technique was used. Nonetheless the potential involvement of the thalamus is of some interest as it has been ascribed a putative role in general attention and wakefulness (Steriade and Conteras 1995) and in the discrimination of painful

stimuli (Lenz *et al* 1995, Mountz *et al* 1995). Such ideas have been developed to hypothesise that the thalamus acts as an information modulator in transmission of sensory stimuli to the cortex (Sherman and Guillary 1996). Although such hypotheses are appealing it must be emphasised that they are theoretical.

Neuroendocrine:

One of the most replicated findings in biological psychiatry is that patients with major depressive disorder have hypercortisolaemia (Goodwin 1998). However, many patients with depression have normal cortisol levels (Berger 1984) and patients with other psychiatric disorders also have abnormalities of cortisol and the hypothalamic-pituitary-adrenal axis (Christie *et al* 1986). As a result of cortisol's central role in the stress response there has been interest in whether abnormalities in the HPA axis may be linked to MUS. In particular is the link between distress and unexplained symptoms via the final common pathway of the HPA axis.

Initial findings in chronic fatigue syndrome (Taerk *et al* 1987) and fibromyalgia (Hudson *et al* 1984) suggested that the neurobiology of MUS may differ from depression and that hypercortisolaemia was surprisingly uncommon. Further evidence came from fatigue states post glandular fever where low, not high, cortisol was noted (Isaacs 1948, Kleinman and Strauss 1993). This was later replicated in chronic fatigue syndrome (Poletiakoff 1981). More comprehensive investigations led to the conclusion that there was mild, centrally induced, adrenal

insufficiency which was secondary to reduced corticoptrophin releasing factor the cause of which was unknown (Demitrack *et al* 1991).

Similarly in fibromyalgia researchers have found low 24 hour cortisol levels (McGain and Tilbe 1989, Crofford *et al* 1994) and blunted cortisol response to CRH stimulation (Crofford *et al* 1994) or insulin-induced hypoglycaemia (Greip *et al* 1993). An alternative mechanism for disruption of neuroendocrine function has been suggested following findings of reduced insulin-like growth factor (IGF-1) in fibromyalgia (Bennett 1992) and post-polio syndrome (Gupta *et al* 1994). This offers potential links between sleep disturbance and functional muscle symptoms via disruption of the growth hormone axis. Unfortunately, not all attempts at replication have been confirmatory (Buchwald *et al* 1996).

HPA axis dysregulation may be linked to underlying problems in serotonin pathways. In studies using dynamic challenges to central receptors it has been found that in medication free CFS patients with no depressive symptoms there was an elevated prolactin response to challenge with d-fenfluramine. A comparison group of normal subjects were indeed normal and a comparison group of depressed subjects showed a blunted response (Cleare *et al* 1995). This finding has been subsequently replicated (Sharpe *et al* 1997). It is suggestive of increased 5-HT activity which is acting to decrease cortisol levels, although it is possible that it is the reverse that is occurring and 5-HT is being up-regulated as a result of low cortisol. It is unlikely that mood is a confounding variable as the opposite

effect would be expected in depression, but disrupted sleep or social routine may be a potential explanation (Lesses *et al* 1996).

Findings of serotonergic abnormalities are of particular interest as they have been reported in numerous other MUS syndromes including irritable bowel (Dinan *et al* 1990, Gorard *et al* 1995), all pain syndromes (Hampf 1989), non-ulcer dyspepsia (Chua *et al* 1992), fibromyalgia (Molodofsky and Warsh 1978, Yunus *et al* 1992, Russell *et al* 1992, Houvengal 1990) and premenstrual syndrome (Rapkin 1992).

Immunological:

It has been suggested that the primary mechanisms behind CFS are immunological abnormalities. The major problem is that the studies conducted have lacked clinical and immunologic standardization and failed to realise the relevance of psychological profiles, duration of illness, methodological variation and control group selection (Krupp *et al* 1991). Nonetheless some replicable results have emerged.

Among the more consistent findings have been diminished cellular immune responses, including decreased functioning and low numbers of natural killer cells, and suppression of T-cell proliferative responses to mitogens and antigens (Barker *et al* 1994, Ojo-Amaize *et al* 1994, Caro *et al* 1993). By contrast, humoral immunity is predominantly enhanced in MUS conditions (Barker *et al* 1994, Rasmussen *et al* 1994, Bates *et al* 1995), particularly increases in immunoglobulins and IgG subsets.

However, such patterns of change to immune system are not specific to any one syndrome and have also been described in response to a number of chronic stressful conditions including release from concentration camp, desert survival training, taking exams and spouses of Alzheimers patients (Dekaris *et al* 1993, Buchwald *et al* 1991, Irwin 1994, Gatti *et al* 1994). Animal studies (Stein *et al* 1985) suggest that such immunological changes are associated with inescapable or unavoidable stress.

Nociceptive abnormalities:

Fibromyalgia is the best studied of the MUS syndromes with regard to nociception. Although the precise location of the pain is unclear most evidence points towards the brain or spinal cord (Yunnus 1992). Similarly several studies of irritable bowel syndrome have shown increased visceral nociception, possibly mediated via splanchic afferents to the spinal chord (Whitehead *et al* 1990, Coremans *et al* 1991, Lembo *et al* 1994). Interestingly, studies which formally examine pain thresholds, using thermal stimuli, in MUS syndromes show that general pain tolerance is actually increased (Cook *et al* 1987).

A wide variety of neurotransmitters, neuromodulators and receptors have been associated with the processing of nociceptive information at supraspinal, spinal and peripheral levels. They include serotonin, acetylcholine, noradrenaline, corticotrophin releasing factor neuropeptide Y and opiate peptides as inhibitory factors (Dougherty *et al* 1993, Mjellem-Joly *et al* 1992, Woolf and Thompson

1991) and NMDA, ACTH and tachykinins (primarily substance P) as pronociceptive factors (Kosek and Hansson 1997, Noel and Nemeroff 1987).

Although hypotheses have been developed around all these substances there is little confirmatory data on any of them. The possible exception is substance P which has been demonstrated to be three times higher in fibromyalgia patients than controls (Russell *et al* 1994, Vaeroy *et al* 1988). However it is not clear whether this finding is the cause of pain or the result of pain.

Autonomic dysfunction:

There are identifiable autonomic nervous system abnormalities in many of the MUS syndromes. The most consistent finding, certainly in fibromyalgia, has been an impaired sympathetic ability to respond to a stressor (Elam *et al* 1992, Qiao *et al* 1991). Furthermore, studies in irritable bowel (Mayer and Raybould 1990, Lynn and Friedman 1993) and migraine (Pogacnik *et al* 1993, Appel *et al* 1992) suggest that there is a disassociation between the symptoms of pain and of autonomic function. This supports hypotheses that propose the axes of the stress response are independent.

Related to autonomic dysregulation is the phenomena of smooth muscle dysmotility. This has been observed in many MUS syndromes but is most studied in irritable bowel syndrome (IBS). Not only do such patients have smooth muscle dysmotility in their intestines but also throughout the rest of their bodies including bladder, lung and oesophagus (White *et al* 1991, Kellow *et al* 1992, Whorell *et al*

1986, Kellow *et al* 1987). Similar changes have also been noted in fibromyalgia (Clauw *et al* 1996).

Psychological hypotheses

Psychodynamic theories:

Early psychodynamic theories were described in the historical review. Over the last thirty years there has been a shift in focus from Freudian drive theories to object relations models which examine development of the self. Within such a model it is hypothesised that deficiencies in the early mother- child relationship leave the individual with structural psychic deficits and an inability to use the imagination and language to contain distressing and unbearable feelings. This results in a paucity of fantasy life, dream experience and emotional responses which turn leads to an increased susceptibility to somatic complaints (Guthrie 1995). Within such a hypothesis it is recognised that there is a spectrum of severity with some individuals who have had *good enough* care (Winnicott 1958) during childhood but develop somatic complaints in response to temporary stressors. Nonetheless, they are able to maintain essentially healthy relationships and the resolution of the problem can occur with recognition and change within the individual. At the other end of the spectrum there are individuals who have had highly abusive upbringings with marked emotional deprivation. Their relationships, by contrast, are chaotic, fragile and often symbiotic. This latter term suggests that they often find partners who are also unable to form mature relationships and that they both manage to fulfil their psychic needs via the dysfunctional dynamics of their relationship. In MUS, the 'invalid' is often cared

for by an overly sympathetic or dutiful partner. As this situation acts as a conduit for intolerable emotional feelings for both partners any change to the nature of the relationship will be fiercely resisted (Guthrie 1995). Brook and Bingley (1991) and Pilowsky (1985) have both cited this as a factor in patients refusing to work with psychotherapists.

As with most psychodynamic theories this is difficult to confirm or repudiate. There is evidence that poor childhood experiences are associated with increased frequency of somatic symptoms in adulthood (Hotopf *et al* 1998, Craig *et al* 1994). This does not necessarily confirm the dynamic hypotheses as Craig *et al*'s work also suggests that childhood modelling in the form of exposure to illness experiences may be of particular importance. The evidence cited by the St Louis group (Guze *et al* 1971, Cloninger *et al* 1975, Cloninger *et al* 1986) of an excess of alcoholism and psychopathy in the family backgrounds of severe somatizers could be reinterpreted in line with this theory. Thus, it is not evidence of a genetic link but a marker of poor child rearing practices. There is also evidence that adults with chronic intractable pain are more likely to have been hospitalised as children (Pilowsky *et al* 1982) and there is often similarity between the children's symptoms and those of their parents. Family members with physical handicap or deformity may be potent models for future somatization (Blumer and Heilborn 1981, Hartwig and Sterner 1985). Furthermore there is evidence that particular types of traumatic experience in childhood may guide the symptoms displayed as an adult. In particular, pelvic pain and unexplained abdominal pain are more

common in women who have been sexually abused (Drossman and Thompson 1992, Walker *et al* 1992).

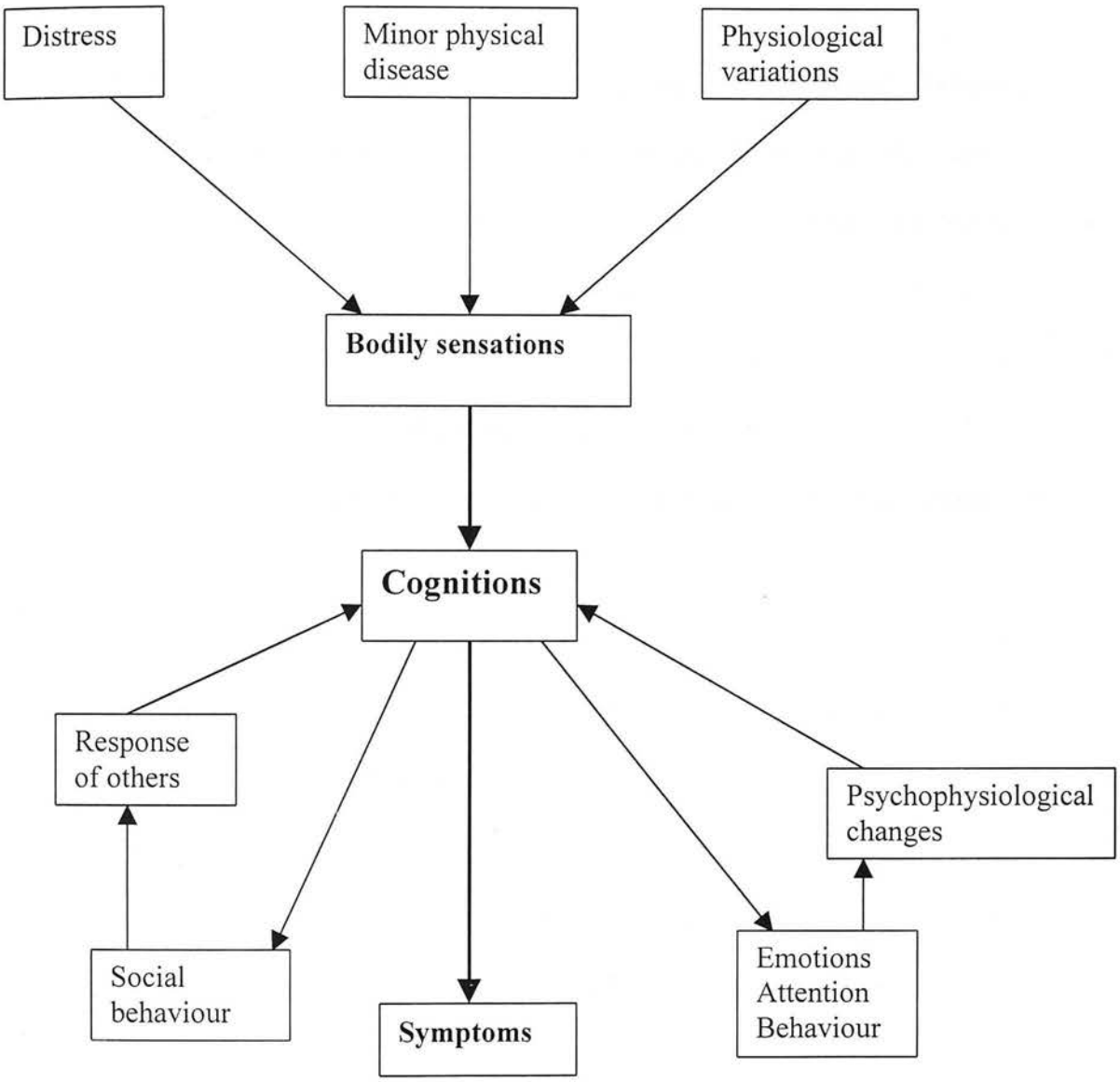
Evidence in keeping with the aetiological significance of recent traumatic events has been provided by Creed (1990) in a model of irritable bowel syndrome in which stressful life events can play both a primary and a secondary role in symptom amplification. Pennebaker *et al* (1988) have shown that how a subject interacts with stressful life events is of importance, and inhibition of emotions and lack of confiding may cause physiological arousal, somatic symptoms and disease (Pennebaker *et al* 1988, Pennebaker and O'Heeron 1984).

Psychodynamic theories can also be useful tools for examining the clinical encounter. Doctors often complain that patients with MUS are more difficult to deal with (Lin *et al* 1991). It has been suggested that such feelings have their genesis in the doctor's awareness of their own inadequacy in diagnosing and treating the patient's illness (Corney et al 1988, Goldberg et al 1992). However it may be that the genesis of the emotion lies not in the doctor but in the patient and the patient is able to engender within the doctor some of their own confusion and fears of disintegration. Such a transfer of primitive emotions has been well described within the context of projective identification (Segal 1973). Whether or not such dynamic explanations are accepted it is undoubtedly better to have a structure within which to examine such emotions rather than respond unwittingly via heroic over-treatment or by using discharge as a punitive measure.

Cognitive behavioural theories:

Cognitive behavioural theories have their roots in learning theory which has traditionally served as an important bridge between experimental psychology and clinical psychiatry (MacKay 1992). Learning has been defined as "the change in a subject's behaviour brought about by the subject's repeated experience in that situation." (Bower and Hildegard 1981). Cognitive behavioural theories encompass both *stimulus-response* theories (classical and operant conditioning; Bower and Hildegard 1981) and *cognitive theories* (social modelling; Rosenthal and Bandura 1978). The more recent development of cognitive behavioural therapy can be largely attributed to the work of Beck (1979). The basic tenant is that a patient's thoughts and beliefs may not be a consequence of their emotional state but rather the cause. The model attempts to break down experiences into four inter-related components of cognition, emotion, behaviour and physiology (Hodgson and Rachman 1974). Central to the theory is that a patient's cognitions are of primary importance in determining their behaviour and their emotional and physiological state (Lishman 1988, Salkovskis 1989; see figure 6.1). In this model the cognitions will determine the consequences of the various inputs including bodily sensations, minor physical disease and physiological variation. In the development of MUS an initial early response to input from one of these stimuli can be emotional distress. This in turn may cause further bodily sensations. Increased attention may then be paid to these sensations resulting in their amplification. At this level, behavioural interactions can be influenced by cognitions and a number of different responses generated. Whilst some responses may be helpful, others may act to exacerbate the problem rather than to relieve it.

Figure 6.1. **The cognitive behavioural model of medically unexplained symptoms (Sharpe et al 1992).**



Additionally, others, such as family members or doctors, may input into the system by acting in a way that intensifies rather than reduces the concern with disease (Sharpe *et al* 1992).

Within this model it is recognised that the awareness of bodily sensations varies between individuals (Tyrer 1976) and can be increased by the belief that they signify danger or disease (Salkovskis 1990). Misattributions of this type can be influenced by specific fears about physical health and functioning (Robbins and Kirkmayer 1991). The more one believes that one has a disease, the greater the focus of attention on the body and the more symptoms are perceived; such amplification can be self perpetuating in a vicious cycle (Skelton and Pennebaker 1993).

Emotional distress and anxiety often give rise to physical symptoms in their own right. Depression is classically associated with reduced energy and muscular pain (Simon 1990, Stoeckle 1962). Anxiety, by contrast, causes increased activity in the sympathetic nervous system resulting in tachycardia, shaking and sweating (Tyrer 1976, Tyrer *et al* 1980). Dysfunctional responses include repeated checking and reading the medical literature. This can lead to preoccupation with symptoms and the sinister reinterpretation of sensory signals. Dysfunctional behaviour can be avoidant as well as active. This could include avoiding physical activity for fear of provoking symptoms (Phillips 1987), taking time of work, avoiding social activities and reducing exercise. Such responses can cause physiological adaptation that serves to worsen the original complaint (Salit *et al*

1986). Interpersonal factors can influence this by reinforcing emotional distress, preoccupation with disease and symptom maintaining behaviour (Benjamin *et al* 1992). Even such actions as repeated reassurance generally serves to worsen morbid concerns (Warwick and Salkovskis 1985). Doctors in particular, via the circumstances of their contact with patients, have the propensity to generate and unintentionally perpetuate the patient's distorted views of their symptoms (Bergman and Stamm 1967).

Negative Affectivity:

Although not directly aimed at the study of MUS, Clark and Watson's (1991) concept of negative affectivity (NA) is of relevance to the aetiological discussion. There model sets out to explore the psychometric evidence for and the taxonomic implications of the diagnosis of the syndromes of depression and anxiety. Their method involved a review of all the main rating scales for syndromes and an examination of their convergent and divergent validity, and their inter-rater reliability. They suggest that the data is best explained by a tri-partite model of a general distress factor (negative affectivity; NA) and specific factors for anxiety and depression. As non-specific trait for distress, NA can be shown to be stable over time (Clark and Watson 1991a) and show significant heritability (Clark and Watson 1991a). It is hypothesised that this non-specific factor may be the mechanism between the trait of an individual subject being prone to physical symptoms and emotional disorders and the individual state diagnoses of MUS, depression or anxiety.

Ambiguity:

Unexplained symptoms are, by definition, associated with ambiguity. This is problematic as it allows a wide variety of ideas, beliefs and fears to flourish. Many of these may be inaccurate and some actively unhelpful. In a study of American soldiers suffering from fatigue and emotional disorders due to a mysterious infection it was found that psychological factors impeded recovery. Those soldiers who displayed anxiety, ignorance, lack of trust in doctors and a feeling that they would never recover had a poorer prognosis. This was despite the fact that it was later found that all the soldiers had infact contracted schistosomiasis (Frank 1946). Thus, irrespective of the actual cause, patients' interpretation of the pathology and prognosis can have a determining effect on outcome. This has also been found in unexplained symptoms, particularly patients with chronic fatigue. Several studies have found that an active belief in an exclusively physical model of ME is associated with worse outcome (Wilson *et al* 1994, Vercoulen *et al* 1996).

For patients with MUS the ill-defined nature of the symptoms and the lack of diagnostic label are clearly problematic. In the absence of an explanation patients can either blame themselves or, alternatively, blame others for not finding the cause. Thus patients with fibromyalgia display apprehension about the unknown pathology, a distrust of doctors for being unable to explain the condition and a self-doubt that others will belief the intensity of the pain (Gaston-Johansson *et al* 1990, Robbins *et al* 1990). This leaves the patient requiring a plausible explanation in the dominant societal model, ie pathobiological, for their disability

(Suraway *et al* 1995, Woodward *et al* 1995). Indeed, the need to preserve self-image and deflect blame for any suggestion of complicity in the symptoms can result in patients posturing as super-normal. The type that others come to with problems and definitely not 'the type to get depressed'.

Social models:

The major social models describing MUS have been discussed in the previous chapter. However, it is worth examining how the personal attributions discussed in the previous section have also been displayed at a societal level. In a well written essay *CFS: a social history of twentieth century disease* Wessley *et al* (1998) describe the context within which the scientific debate over the aetiology of chronic fatigue has been conducted. The CFS story was in some ways unique as the anti-psychiatry aspects of the user movements for ME were pre-emptive and began before psychiatry had taken an interest in the disorder. In short the 'victim of a germ infection is blameless' (Helman 1978), but a psychological disorder 'implies weakness or lack of moral fibre' (Seagrove 1989). Whilst such debates have existed since Sydenham changed medicine to a disease centred, patho-biological model, what was new was the orchestrated public strategies used against any suggestion that fatigue could be a psychological disorder. Organised campaigns were conducted via the Internet and other media to discredit psychiatric research and, also psychiatric researchers. Available evidence was denied and psychiatric terms were altered (ie antidepressants became immunomodulators). From the patients' perspective, it should be noted that although the majority object to psychologisation because they consider that it

equates with imaginary disease or madness for some it also carries real practical consequences such as being denied health insurance (Stopp 1993).

The role of the media in this debate has been of major importance. They have raised awareness, and concern, about the role of various toxins, chemicals, pollutants and vaccines in our lives and how they have created diseases (Lees-Haley *et al* 1992, Roht *et al* 1985). Whilst this may have helped influence the terminology patients used to describe their symptoms it would be simplistic to think that it had caused them de novo. Indeed, many patients have been actively grateful that the media have brought sense to otherwise mystifying groups of symptoms (Clements *et al* 1997). Nonetheless, journalists may be guilty of renaming the already known in search of the next story (Jones 1987) and are certainly guilty of creating polarised accounts of aetiology when by definition MUS must encompass uncertainty. In fact many journalists see it as their duty to promote consumerism in the face of medical paternalism (MacLean and Wessley 1994). Thus the aetiology of unexplained symptoms is discussed in terms of populist conceptions of current scientific models; as they always have been. This has allowed a causative role in the development of symptoms for over-prescription of antibiotics leading to altered immunity, food allergies, vaccines, viral variants of HIV, candida infection, electromagnetic sensitivity, sick-building syndrome, dental amalgam, leaking silicon breasts, and chemical sensitivity (Stewart 1990).

Along with this rise in medical consumerism has come disease activism. Intense lobbying by patient groups has led to research programmes whose sole aim is to 'legitimise the disorder' and their success is judged by their presence not by the benefits of their findings. Thus the *Wall Street Journal* (1990) described the Atlanta Center of Disease Control's study into CSF (Gunn *et al* 1993) as having 'one major goal.... To replicate the experiments showing that people with the condition suffer from immune system irregularities and not psychiatric troubles'. Not all research is viewed as helpful to the cause and lobbyists fight just as hard to prevent psychiatric research into MUS syndromes; tactics such as anonymous denunciations and allegations to charities, government institutions and medical journals are used in order to attempt to subvert funding or publishing of research. Lest there be any doubt about the passions involved Paul Cheney, a prominent US physician and ME sufferer said ' we who believe that this is a real disease are almost in a death grip with the forces that would stifle debate, trivialise the problem and banish patients who suffer from it beyond the edges of traditional medicine' (Fields 1990). Likewise in Britain, Masefield (1994) likened ME to the plight of the Beirut hostages or Nelson Mandela's imprisonment. It would be easy to ignore such statements or to dismiss them with feelings of exasperation and irritation, but if sensible, balanced work is to take place then the doctor must be aware of the wider context within which the consultation is taking place. The patient may no longer be coming for an opinion but, instead, coming with an opinion. To ignore or dismiss this out of hand will help neither the patient or the doctor.

Litigation:

A putative role for litigation in the social aetiology of MUS has long been suggested and came to prominence in the nineteenth century with *railway spine* (see previous chapter). The twentieth century equivalent, whiplash injuries from motor vehicle accidents (MacNab 1964) has attracted similar interest. This intensified after it was found that there was a dramatic reduction in whiplash claims in Victoria, Australia following the introduction of legislation limiting court actions and compensation (Ferrari and Russell 1999). The reasons for the reduction were unclear but were believed to include many factors beyond medical need including financial gain and the desire for retribution (Reilly *et al* 1991). In addition, there is evidence of reduced incidence of whiplash in jurisdictions where there is little expectation of symptoms, disability or compensation (Balla 1982, Schrader *et al* 1996). In Saskatchewan, Canada, the province's tort system of compensation was changed to a no-fault system in 1995. In an examination of the impact of this on the outcome of whiplash injuries, Cassidy *et al* (2000) found that, despite similar baseline characteristics for the claimants, those who settled under a no-fault system closed much faster. Furthermore, there was a strong and consistent association between time to closure and recovery from injury. By the time of settlement, those who closed quickly, suffered less pain and had higher levels of physical function despite having similar disability levels at baseline assessment.

6.5. Detection, management and treatment.

Although prevalence studies have consistently reported that around half the patients presenting to general practitioners have unexplained symptoms, whether this is actually detected is more open to question. It is well recognised that primary care doctors only diagnose mental disorders in around one third to a half of patients who actually present with them (Bridges 1985, Munk Jorgensen 1997). However such research has concentrate on depression and anxiety states and there is a paucity of information about the detection of MUS. Fink *et al* (1999) examined this in Aarhus, Denmark. They found that general practitioners detected from 50% to 71% of patients with ICD 10 somatoform disorder, and between 36% to 48% if DSM criteria were used. There was no evidence of bias by age or sex. Such rates are in keeping with the detection rates for depression and anxiety. In secondary care settings, Nimnuan *et al* (2000) showed that it was failure to diagnose MUS when present, rather than the missed diagnosis of an 'organic' cause, that was the major source of clinical error.

The desirability of detection and diagnosis of MUS by clinical history and physical examination is well demonstrated by Kurt Kroenke. He examined 1 000 consecutive case records from ambulatory care in the United States (Kroenke 1989). His results are described in Figure 6.2 and Table 6.2. Few symptoms had an organic cause and investigations had a very high cost for a very low yield. The theme of health care utilisation has been developed by several authors. Although one might assume that those who lack a pathologically based disease will not consume many resources, anyone who has been involved in the care of

Figure 6.2. **Three year incidence of 10 common symptoms and the proportion of symptoms with a suspected organic cause (Kroenke *et al* 1989).**

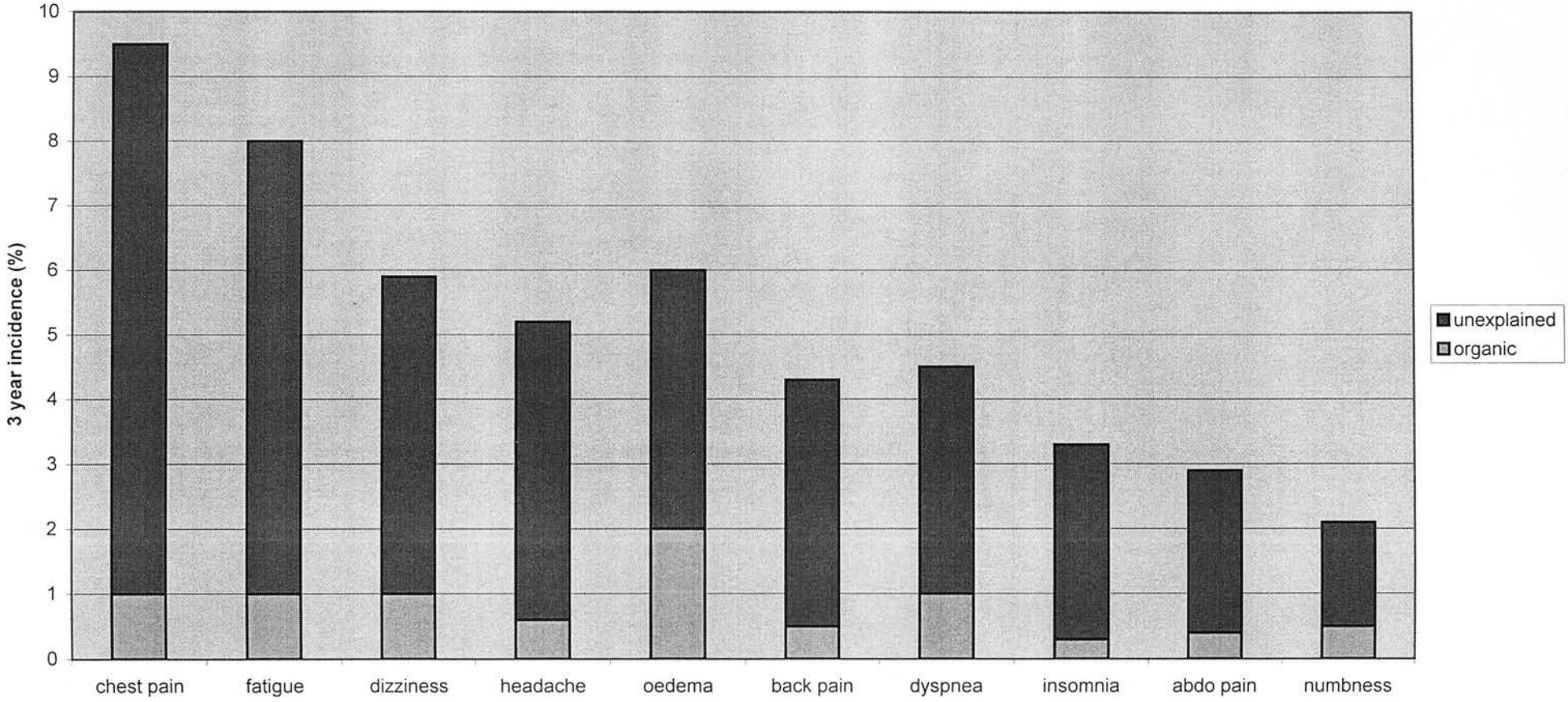


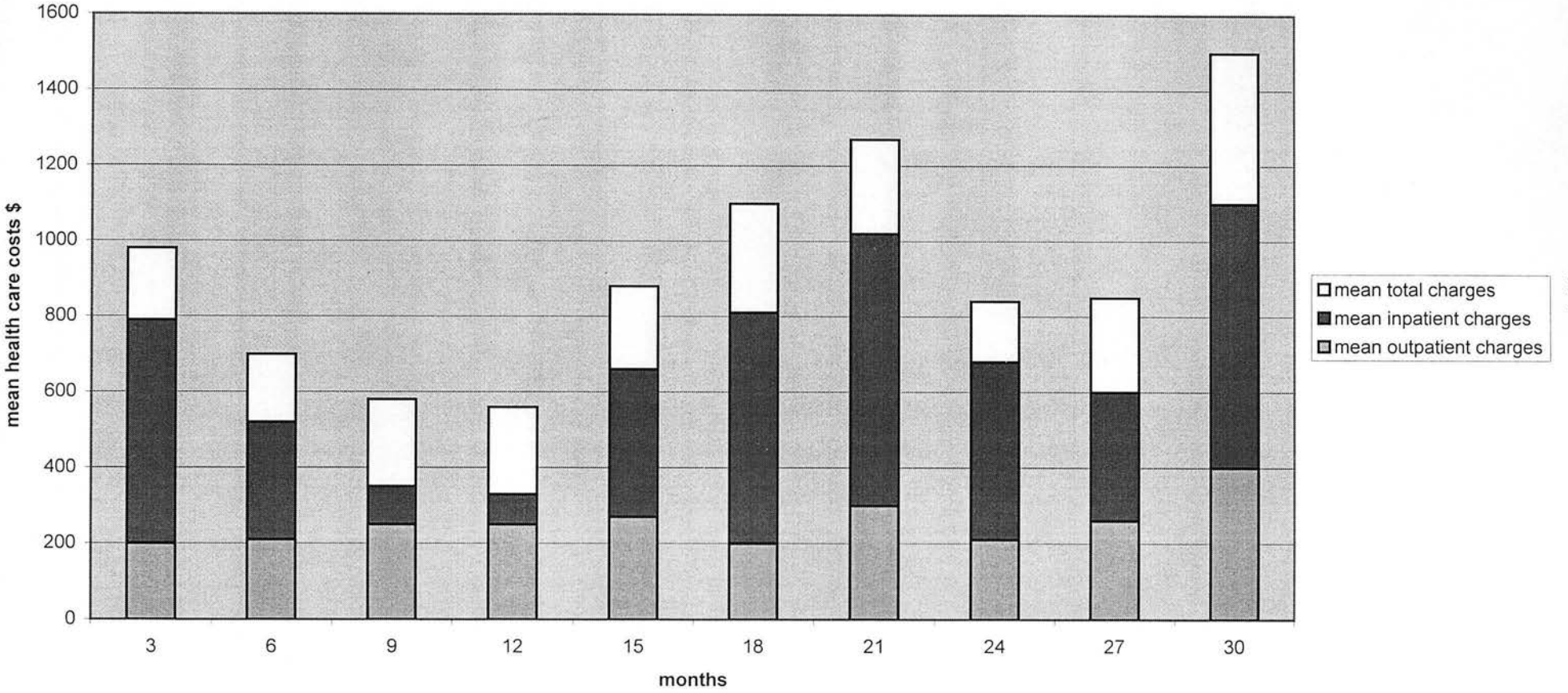
Table 6.2. **Diagnostic evaluations of 14 common symptoms (Kroenke et al 1989).**

Symptom	Number evaluated	Number of organic diagnoses discovered by testing	Estimated cost ($) per evaluation	Estimated cost ($) per organic diagnosis
Chest pain	80 (83)	5	272	4 354
Fatigue	57 (70)	5	130	1 486
Dizziness	34 (62)	3	223	2 532
Headache	20 (38)	1	389	7 778
Oedema	26 (58)	4	122	793
Back pain	31 (76)	1	234	7 263
Dyspnea	31 (84)	9	209	720
Insomnia	6 (18)	0	110	-
Abdominal pain	27 (90)	3	202	1 816
Numbness	17 (65)	2	160	1 364
Impotence	13 (54)	2	160	1 364
Weight loss	18 (100)	0	325	-
Cough	15 (100)	2	147	1 104
Constipation	7 (58)	0	409	-
total	382 (67)	37	218	2 252

patients with MUS knows that, certainly at the severe end of the spectrum, this is not the case. The scale of health care utilisation in US primary care by patients with MUS has been described by Smith *et al* (1986). They found that such patients cost a mean of $ 4 700 per annum compared to the national per capita average of $ 543. A breakdown of these costs is described in figure 6.2. In Europe, Fink *et al* (1999) showed increased health service utilisation by patients with ICD 10 somatoform disorder. Their results were not as dramatic, reflecting a less restrictive definition of MUS, but still showed an increased use of both primary and secondary care resources compared to a random sample of GP attenders.

The need for treatment is clear, both in order to alleviate patients' suffering and in order to make the best use of available health care resources. However, the provision of effective treatment is not without its difficulties. As the previous section showed, current models of unexplained symptoms are various and range from narrow biological aetiologies requiring medical therapy to purely psychological explanations best treated with psychotherapy. Patients often favour the former whereas the evidence of treatment efficacy often lends support to the latter. A good example is the conflicting conceptualisation of chronic fatigue syndrome in which patients typically see their illness as medical (Wessley *et al* 1998) whereas the most clearly evidence based treatment is cognitive behavioural psychotherapy (Price and Cooper 2000).

Figure 6.3. **Mean health care charges per patient in 41 patients with somatization disorder tabulated per quarter (Smith *et al* 1986)**



Both clinical experience and research suggest a resistance to accepting suggestions that their somatic symptoms are entirely mental in origin is a characteristic of many patients with somatic complaints that are medically unexplained (Salmon *et al* 1999). Why should this be? A number of explanations may be considered but a likely important one is that Western dualistic metaphysics (see chapter 5) leads to illnesses that are conceptualised as 'mental' being regarded as 'not real', implying weakness, fault or loss of reason on the part of the patient and consequently being stigmatising (Kirmayer 1988). Understandably therefore, rather than clamour for psychiatric treatment, patients have continued to attend physicians and insisted on general medical care.

For their part increasingly biomedically orientated specialist physicians have either obliged them with extensive but often unproductive medical investigation (Fink 1992) or perhaps more commonly, regarded them as having 'psychiatric problems. Neither approach has been notably successful. Patients have consequently been left in a 'no man's land' between a psychiatric approach they reject and a narrow biomedical approach that often rejects them (Quill 1985). Perhaps understandably many have turned to the largely somatic explanation of 'alternative medicine (Astin 1998, Dimmock 1996).

Current evidence based management:

Currently recommended treatment approaches can be divided into general and specific components:

General management strategies:

Those clinicians with a special interest in the area have offered principles of general management, based largely on clinical experience (Bass and Benjamin 1993, Barsky 1998). These are outlined in table 6.3.

There has been surprisingly little evaluation in clinical trials of the effectiveness of components of the general management of patients with unexplained somatic symptoms. The negative effect of excessive investigation has been much lamented but little studied (Todd 1984). Trials of limiting hospital referral from primary care for patients with multiple chronic unexplained symptoms have yielded evidence of cost savings but only marginal improvements in the patient' s condition (Smith *et al* 1986, Rost *et al* 1994).

Ther has also been little study of the effect of how the physician explains the nature of medically unexplained symptoms to the patient. There is certainly evidence that iatrogenic harm may be caused, for example by suggesting to the patient they are sick when they are not (Bergman and Stamm 1967). Much less attention has been given to the study of positive messages. One trial from British general practice compared the effect of giving a positive explanation, indicating that the physician understood the nature of the complaint, to patients attending with minor unexplained symptoms to that of giving none. Those who received the positive explanation had a better outcome (Thomas 1987).

Table 6.3. **General management strategies for patients with unexplained somatic symptoms**

Exclude medical conditions but avoid unnecessary investigation or referral

Seek specific treatable psychiatric syndromes

Demonstrate to the patient that you believe their complaints

Take a full and sympathetic history

Establish a collaborative relationship

Give the patient a positive explanation but do not over-emphasise psychological factors

Encourage a return to normal functioning.

Specific management strategies:

There has been much more systematic examination of the effectiveness of specific therapies in patients with a variety of unexplained syndromes. In particular, there is considerable evidence to support the 'psychiatric treatments' of antidepressant drugs and psychotherapy.

Antidepressant drugs:

A recent systematic review of antidepressant therapy for such syndromes found them to be moderately effective overall (O'Malley et al 1999). Ninety-six randomised trials were reviewed. These used a variety of antidepressants in a number of different MUS syndromes (table 6.4).

The authors concluded that there was evidence for the effectiveness of a variety of antidepressant drugs. The odds ratio for improvement with antidepressant treatment compared to placebo was 3.4 and the effect size was similar across syndromes. However, the high dropout rate from treatment, even in this selected sample, indicates that the acceptability to patients in practice is not well established.

Cognitive behaviour therapy:

The psychological therapy most commonly recommended is usually a form of behavioural or cognitive behavioural therapy (CBT). This is an explicitly psychological treatment that aims to achieve recovery by helping the patient

Table 6.4. **Syndromes (and number of trials in each) included in a systematic review of antidepressant drug treatment (O'Malley *et al* 1999).**

Headache: migraine (34) tension headache (18)

Fibromyalgia (18)

Functional GI (11)

Idiopathic pain (11)

Tinnitus (2)

Chronic fatigue (2)

change illness perpetuating beliefs and behaviours. A recent systematic review of CBT in patients with unexplained symptoms (Kroenke and Swindle 2000) has supported the effectiveness of this approach to treatment. Twenty-nine trials including 27 randomised controlled trials and two non-randomised studies were identified. The syndromes included were slightly different to those included in the antidepressant review (table 6.5).

The heterogeneity of outcome measures made it impossible for the authors to conduct a formal meta-analysis. However, they found that CBT was superior to the comparison condition in reducing symptoms in 70% of trials (table 6.8 and 6.9). Furthermore, the effect on symptoms seemed to be larger than the effect on mood or functioning. As with antidepressant studies most patients were recruited from specialist referral centres and selection biases were assumed to have occurred.

Simple behavioural interventions such as graded exercise have also been studied. Although demonstrating some efficacy these seem to show that such individual behavioural interventions are not as effective as multi-modal CBT. Other components such as attention to psychological factors appears to be required to ensure the acceptability of and adherence to behavioural change, at least in chronic fatigue (Fulcher and White 1997, Wearden *et al* 1998) and low back pain (Nicholas *et al* 1992). Whilst the literature offers good support for the use of CBT in the management of MUS patients in most cases this has been given by 'mental health professionals', in psychiatric settings. Its acceptability to the majority of

Table 6.5. **Syndromes (and number of trials in each) included in a systematic review of CBT (Kroenke and Swindle 2000).**

Back pain (5)

Irritable Bowel Syndrome (3)

Chest pain (3)

Tinnitus (2)

Fibromyalgia (2)

Other symptoms and syndromes (9)

patients attending physicians in medical care settings is not therefore well established.

Iatrogenesis:

Although anecdotal evidence suggests it is common one of the least studies areas in the treatment of MUS is the role of iatrogenesis. In the one of the few studies conducted Kouyanou *et al* (1997) found extensive evidence of misdiagnosis, over-investigation, over-treatment, unhelpful treatment, unhelpful advice and unhelpful attitudes in the management of MUS. Examples included repeating the same negative investigations for reassurance, long-term benzodiazepine prescriptions, advising long-term bed rest, and sceptism about the nature of the patients symptoms. Not surprisingly the patients had high levels of disatisfaction with their care.

6.6. Conclusions.

Medically unexplained symptoms exist in all cultures, ages and both sexes. They are the cause of disability to patients and are associated with increased rates of depression and anxiety. Roughly half the patients with MUS remit spontaneously. The others remain symptomatic and disabled. The relationship between depression and unexplained symptoms is a complex, interdependent one.

There is evidence for a number of aetiological variables and the condition is probably multi-factorial. Evidence suggests a genetic predisposition and abnormal physiological factors coupled with dysfunctional psychological responses leading

to symptom perpetuation. There is also evidence that the social setting in which the symptoms occur is certainly influential on understanding and outcome and possibly influences symptom origin as well.

General aspects of management are little researched and often neglected in practice. Evidence-based specialist treatments exist but psychological therapies are of very limited availability in the medical setting. The best evaluated treatments are 'psychiatric' whilst by and large both patients and physicians prefer treatments seen as medical. There is evidence that patients with MUS may suffer substantial iatrogenic harm, although this area is under researched.

Chapter 7. Medically unexplained symptoms in neurology: a systematic review.

7.1 Introduction

The previous chapters have described the historical and current literature on medically unexplained symptoms. Chapter 5 closed with a description of the controversy caused by Eliot Slater's Shorvon lecture on the 'Diagnosis of Hysteria'. This systematic review of original data studies conducted since 1960 will attempt to examine and answer some of the criticisms that paper raised. It will concentrate on clinical aspects of the study of MUS in neurology and examine the best available evidence in an attempt to answer the following questions. How common are MUS in neurological practice? How accurate is the diagnosis of MUS over time? How disabling are MUS to patients? What is the association of MUS with mood disorders? What is the outcome of MUS in neurology patients? And what are the implications of MUS in terms of health care utilisation?

The results examine cross sectional and follow up studies separately in order to aid comparison between the variety of biases affecting the different study methodologies.

7.2. Results: cross sectional prevalence studies.

The search strategy identified 9 cross sectional prevalence studies of medically unexplained symptoms in neurological settings. The studies' authors, quality, methods and main findings are described in tables 7.1 and 7.2.

Table 7.1. **Systematic review of cross sectional studies of MUS in neurology patients: quality assessment**

Author	year	Case notes only	Prospective Retrospective	Sample defined	control	representative	Objective initial assessment	Initial assessment blind	
Kirk	1976	y	r	-	-	-	-	-	0
Stevens	1989	n	p	+	-	+	-	-	4
Schiffer	1983	n	p	-	-	-	+	-	3
Perkin	1989	n	p	+	-	+	-	-	4
Creed	1990	n	p	+	+	+	+	+	7
Lempert	1990	y	r	+	-	+	-	-	2
Ewald	1994	n	p	+	+	+	+	+	7
Hamilton	1996	y	r	+	+	+	-	-	3
Robertson	1998	y	r	+	-	+	-	-	2
Nimnuan	2000	n	p	+	+	+	+	+	7

Table 7.2. **Results of cross sectional studies of MUS in neurology.**

	subjects	setting	Main measures	Main findings
Kirk 1977	2716	Out patients, neurology, North East England	Case note review	13% had MUS. There was no sex or age difference. 55% of MUS patients had multiple symptoms
Stevens 1989	2284	Out-patients, neurology, Gloucestershire	Clinical diagnosis	6% had 'functional disease'
Schiffer 1983	241	In and out patients, Rochester, USA	DSM-III diagnosis (clinical)	18% had MUS
Perkin 1989	7836	Out-patients, neurology, Charing Cross Hospital	Clinical diagnosis	26% had MUS and further 4% had conversion hysteria
Creed 1990	133	Female in patients neurology, Manchester	Visual Analogue Scale GHQ SPQ IBQ CIS	24% had MUS and a further 34% had some functional overlay of existing organic disease. MUS patients had more symptoms, increased scores on the CIS (75% were 'cases') and SPQ and the hypochondriasis, disease conviction and irritability subscales of the IBQ. GHQ scores were the same in all patients groups. MUS patients had an increased rate of family problems but not of legal or financial problems.

Lempert 1990	4470	In patients neurology, Munich	Case note review	9% had MUS, more common in females, and middle aged. Commenest symptoms were pain related followed by motor symptoms. 38% MUS patients also had depressive diagnosis and a further 13% had anxiety disorders.
Ewald 1994	100	In patients, neurology, Aalborg, Denmark	Visual Analogue Scale SCL-90	14% MUS, a further 26% had mixed MUS and organic disease. MUS patients no different on any demographic data, had increased distress on all SCL-90 subscales except anxiety and hostility. MUS patients believed that psychological factors influenced presentation more frequently than others.
Hamilton 1996	149	Out-patients neurology, Manchester	Case-note review	42% MUS, further 5% no diagnosis
Robertson 1998	350	Out-patients neurology, Cambridge	Case-note review	29% had MUS.
Nimnuan 2000		Out-patients neurology Kings College London	Clinical diagnosis HAD BDQ	21% incorrectly diagnosed as MUS when should have been neurological disease. 43% incorrectly diagnosed as neurological disease when should have been MUS

The sampling frames and methodologies varied between studies. Two, Creed *et al* (1990) and Ewald *et al* (1994) were clearly methodologically superior. Both these studies examined prospectively ascertained, consecutive patient samples. Unexplained symptoms were measured on a visual analogue scale using a continuum of non-organic to organic. Whilst the intra-rater reliability of this method was demonstrated within the studies, the validity of interpretation i.e. where on the line does a symptom become unexplained was open to question. Nonetheless, Ewald's group used the same interpretation strategy as Creed so direct comparison of results was possible. Creed's group, found a prevalence of 24% (95% C.I. 16% to 31%) whilst Ewald's group found only 14% (95% C.I. 8% to 22%). The confidence intervals overlap, indicating that the two groups may only be making different estimates of a true population mean. However, there are more likely explanations for this discrepancy. First, admission policies may be different between Manchester and Denmark. Second, the Ewald study examined first admission patients of both sexes whereas the Creed study examined all patients admitted but restricted the study to females only. Both studies noted that MUS patients had increased rates of distress and in the case of the Creed study 75% of MUS patients reached criteria for 'caseness' on the Clinical Interview Schedule (CIS).

The final study conducted among neurological in-patients, in Munich, by Lempert *et al* (1990) found a prevalence of 9% (95% C.I. 8% to 10%). This study was based on retrospective case note examination and although admirable in scale lacks the reliability of diagnosis that a prospective study can offer.

Of the out-patient studies both Hamilton *et al* (1996) and Kirk and Saunders (1977) aimed to specifically examine rates of MUS in neurology clinics. By contrast, Perkins (1989), Stevens (1989) and Robertson (1998) were all case series reports of neurologists' clinical practice. Unfortunately both the specific studies were retrospective case note examinations. Hamilton *et al* examined the case notes of all patients presenting to neurological clinics and reported a rate of 42% (95% C.I. 34% to 50%) for MUS. Kirk and Saunders (1977) examined only the case records where a primary psychiatric diagnosis had been made or "which could have a psychiatric diagnosis" and found a lower prevalence rate of 13% (12% to 14%). Perkins (1989) and Stevens (1989) had the advantage of prospective ascertainment from personal case series which appear representative of general neurology clinics. Perkins reported a rate of 26% for MUS and a further 4% for conversion disorder specifically (total 30%, 95% C.I. 29% to 31%). Stevens does not comment on MUS as such and suggested a rate of 6% (95% C.I. 5% to 7%) for "functional disease". Robertson *et als* retrospective study of urgent neurology out-patients demonstrated a rate of MUS of 29%.

The study by Nimnuan *et al* (2000) is of interest as it examines misdiagnoses rates from the perspective of both MUS and medically *explained* symptoms. They found that physicians were twice as likely to make an erroneous diagnosis of explained symptoms when the patient had in fact MUS than vice versa. The study was slightly spoilt by the high rates of misdiagnosis in both groups and this was almost certainly down to the fact

that many patients were seen by registrars and senior house officers rather than consultants as in the other cited studies.

The final cited study (Schiffer 1983) described the personal workload of a new neurology intern working in the United States and suggested a prevalence of 18% MUS in patients he saw personally. Although an interesting paper it is difficult to extrapolate from the findings.

7.3. Depression and anxiety disorders in neurology patients.

In addition to the studies cited above three other studies were identified which examined rates of depression and anxiety disorders among neurology patients (table 7.3). De Paulo *et al* (1978), examined 126 consecutively admitted in-patients in the neurology unit at John Hopkins, Baltimore. They found that 50% (58/115) scored above the cut-off for emotional disturbance on the GHQ 30 item scale (Goldberg 1972). Berlin *et al* (1983) examined 105 consecutively attending new out-patients at general neurology clinics in Pennsylvania, USA, using the SCL-90 self report questionnaire (Derogatis 1977). They reported an overall prevalence of 51% for significant "emotional distress" and noted that patients with increased emotional distress reported increased pain. Bridges and Goldberg (1984) examined 100 patients with the GHQ screening questionnaire and followed this with the Clinical Interview Schedule (Goldberg 1984) on those who scored high. They estimated a prevalence of 39% for "psychiatric disorder" of which one third was recognised by neurologists. When they

Table 7.3. **Systematic review of cross sectional studies of depression and anxiety in neurology patients: quality assessment and results.**

Author	year	Case notes only	Prospective Retrospective	Sample defined	control	Objective initial assessment	Self rated or interview	score
DePaulo et al	1978	N	P	+	-	+	SR	5
Berlin et al	1983	N	P	+	-	+	SR	5
Schiffer et al	1983	N	P	+	-	+	SR & I	6

Study	subjects	setting	Main measures	Main findings
DePaulo et al 1978	126	In-patients, general neurology John Hopkins, Baltimore.	GHQ 30- item	50% had emotional distress (defined as scoring over 5 on GHQ)
Berlin et al 1983	105	New out-patients, general neurology, Pennyslvania State University	SCL-90 and neurologists' opinion	51% had emotional distress, all measures 32% as measured by SCL-90 only (defined as score > 70 on at least one scale).
Schiffer et al 1983	100	In-patients, neurology, Manchester	GHQ– 28 item CIS	43% had emotional distress (defined by score >11 on GHQ). 39% had psychiatric diagnosis according to CIS interview.

asked patients whether they would have liked neurologists to inquire about mood symptoms there was an interesting fifty/fifty split between those who thought such enquiries would have been helpful and those who would have regarded it as unhelpful.

7.4. Outcome studies.

The systematic review identified only one outcome study on medically unexplained symptoms in neurology. In addition a further 7 studies were identified (plus one further study which fell outside the specified time frame but which will be discussed) on the outcome of conversion hysteria. Conversion hysteria can be regarded as subgroup of MUS, but the outcome of such patients may not be representative of the much broader category of MUS. The studies and the results are described in tables 7.4 and 7.5.

Jacobs and Russell (1961) retrospectively identified 100 patients with MUS from a consecutive series of case records of newly referred out-patients to neurology in Oxford. They managed to review 92 of these patients five years later. At follow-up there were 5 (5%) instances of undiagnosed neurological disease that explained the presenting symptoms. A further 9 patients had developed other incidental physical disorders not related to their presenting complaint. Twenty six patients (33%) remained symptomatic with MUS although their complaints were described as minor and not disabling.

Table 7.4. **Systematic review of outcome studies of unexplained symptoms in neurology patients: quality analysis**

Study	Year		Defined sample	Control group	representative	Objective initial assessment	Follow up complete	Objective outcome	Outcome criteria blind	
Tissenbaum	1951	R	-	-	-	-	-	-	-	0
Jacobs	1961	R	+	-	+	-	+	-	-	3
Gatfield	1962	R	+	-	+	-	-	+	-	3
Slater	1965	R	-	-	-	-	+	-	-	1
Marsden	1986		-	-	-	-	-	-	-	0
Couprie	1995	R	+	-	+	-	+	+	-	4
Mace	1996	P	+	-	-	+	+	+	-	5
Crimlisk	1998	R	+	-	-	+	+	+	-	4
Binzer	1998	P	+	-	-	+	+	+	-	5

Table 7.5. **Systematic review of outcome studies of medically unexplained symptoms in neurology patients: main findings**

	n	Setting	Follow up (years)	Main findings
Tissenbaum 1951	395	in-patients, psychiatric, New York (Veterans administration)	4	13.5% cases had misdiagnosed organic disease. Incorrect dx commonest with Parkinson's disease and multiple sclerosis
Jacobs 1961	92	out-patients, neurology, Oxford	4 to 6	5% cases misdiagnosed organic disease. A further 10% had developed unconnected organic conditions. Of those with MUS, 33% remained symptomatic
Gatfield 1962	24	In patients, neurology, St Louis	3 to 10	21% cases had misdiagnosed organic disease. 1 subject was classed as malingering and 1 had an anxiety disorder. Of those with MUS 59% remained symptomatic
Slater 1965	85	National Hospital, Queens Square, London	7 to 10	39% had misdiagnosed organic disease. 28% had had organic disease with functional overlay diagnosed at first assessment. 39% still no organic explanation for symptoms (although in 11 subjects symptoms of psychiatric disorder emerged). Of those still classed as MUS 38% were severely disabled by their symptoms
Marsden 1986	34	National Hospital, Queens Square, London	unspecified	44% cases had misdiagnosed organic disease.

Couprie 1995	56	In patients, neurology, Utrecht	4.5	2 patients had misdiagnosed organic disease. (cerebral infarct and multiple sclerosis). 59% remitted completely or had minor symptoms. 41% remained disabled by symptoms. Good prognosis associated with recent onset of symptoms and improvement during initial stay in hospital
Mace 1996	73	National Hospital, Queens Square, London	10	15% patients had misdiagnosed organic disease (although the possibility of an organic explanation was raised at initial assessment in 6 of these cases). 59% of patients improved and in 22 cases remission was complete. 30 (41%) cases showed no improvement or got worse. Patients with affective disorder had better prognoses, patients with personality disorder did worst.
Crimlisk 1998	64	National Hospital, Queens Square, London	6	5% patients had misdiagnosed organic disease (spinocerebellar degenration, paroxysmal hemidystonia and myotonic dystrophy). 48 % had improvement52% remained unchanged or got worse.50% were either medically retired or on long-term sick pay. 75% had co-morbid psychiatric disorders.
Binzer 1998	30	In patients, neurology, Umea, Sweden	2 to 5	No cases of unexpected organic disease. 53% had complete remission. 27% had partial improvement and 10% were worse. Personality disorder and poorer health status at initial assessment were associated with poor outcomes.

Of the studies that specifically examined conversion hysteria, it was notable that despite all the studies being labeled as follow-up or outcome studies only two, Mace and Trimble (1996) and Binzer and Kullgren (1998), actually used a prospective methodology. Mace and Trimble conducted a ten year follow up of patients who had been diagnosed with hysteria following referral to the liaison psychiatry unit at the National Hospital, Queens Square, London. Although the patients were identified consecutively, and examined using standardised measures, the Liaison Psychiatry Department of a tertiary referral hospital can only be regarded as having unique sample which may not be representative of patients from other centres. In 43 (58%) of their patients symptoms had improved by time of follow up and in 22 of these cases they had remitted altogether. The other patients had remained the same or got worse. Neurological disease which explained the patients' symptoms had occurred in 11 (15%) cases. However, in six of these cases a provisional neurological diagnoses had been made at the time of study enrollment and the follow-up only served to confirm this. It should be noted that the symptomatic outcome remained the same or got worse in 9 of these 11 cases, despite the change in diagnosis. In only two cases, one of myasthenia gravis and one of laryngeal carcinoma did the change in diagnosis lead to an improvement in patient outcome. When the outcome of the whole sample was examined initial measures of mood, personality or illness behaviour failed to be of any prognostic value.

Binzer and Kullgren (1998) followed up 30 consecutively identified in-patients, diagnosed with DSM IV motor conversion disorder in the Neurology Department of Umeå University Hospital, Sweden. They excluded patients with co-morbid somatization disorder, patients with symptoms of more than 3 months duration and patients with co-morbid post traumatic stress disorder, leaving a very pure but perhaps unrepresentative sample. Nineteen patients completely recovered during the two to five year follow up period, most within the first six months. Of the other eleven patients, 8 had improved but were still symptomatic. There were no cases of unexpected neurological disease being diagnosed at follow up. Poorer outcomes were associated with Cluster C personality disorders, concomitant physical disease and poorer overall functioning but not with measures of emotional distress, illness behaviour or attitudes.

The other studies all used retrospective case note ascertainment to define their cohorts. Methodologically Couprie *et al* 1995 and Crimlisk *et al* 1998 were superior studies. However, both suffered from having to rely on a clear statement being made in the case notes that the patient had conversion disorder. The Crimlisk *et al* study was of particular interest as it also demonstrated the validity and reliability of the use of a four point scale for rating 'organicity' of presenting complaint. Both studies examined in-patients in tertiary referral institutes, although one might suspect this caused less bias in the Couprie *et al* study where more of the patients appeared to be routine referrals. In the Crimlisk *et al* study there was a high proportion of white, social class 1 patients with medical backgrounds. Nonetheless, both described similar results with low rates of

misdiagnosis (Couprie *et al* 4%, Crimlisk *et al* 5%) and high rates of ongoing morbidity. In both studies approximately half the patients remained disabled by their symptoms at the time of follow-up. The Couprie *et al* study had the added benefit of being the only study to use an objective outcome measure for disability; a modified Rankin scale (Bamford *et al* 1989). At follow up 32 patients were grade 0 or 1, 13 patients were grade 2 or 3 and 9 patients were grade 4 or 5. They also found that initial early improvement, whilst in hospital, was such a strong predictor of outcome that no other characteristics added additional information. Crimlisk *et al* associated good outcome with shorter symptom duration, the presence of a mood disorder and, most importantly, change in marital status. Poorer prognosis was associated with personality disorder, receipt of benefits and ongoing litigation.

Of the early studies Gatfield and Guze 1962 was methodologically superior to Slater 1965 and Tissenbaum et al 1951. Gatfield and Guze 1962 identified 37 in-patients who had been discharged from the neurology unit at St Louis with the diagnosis of conversion hysteria between 1950 and 1957; 24 were followed up. There were four (17%) cases where neurological disorders were judged to have been the cause of the presenting complaint. In two of these cases the patients had pre-existing disease (neuro-syphilis and a temporal lobectomy for carcinoma) and the conversion disorders were judged, wrongly, to have be superimposed on these pictures. The follow up period demonstrated that the original disorders were probably the cause of all symptoms. One of the remaining two cases was of missed "basal ganglia disease" and the other

developed marked wasting of one leg, and hyper-reflexia with associated symptoms of intermittent abdominal pain and vomiting for which no explanation was found. A further patient was later diagnosed with malingering and another patient with an anxiety disorder. Of the 18 patients left, 11 (61%) were still symptomatic and the other 7 had complete remission. Both Slater and Tissenbaum *et al* are, by modern standards, fatally flawed studies. Both lack any real definitions for entry criteria, sampling frames, or outcome measures and it is therefore difficult to interpret what the relevance of the data actually is. In the Slater study "hysteria" was often being used to describe a histrionic reaction to organic disease. Given that the patients had identified neurological disease at entry to the study, it is no surprise that they still had identified disease at follow up. The Slater study is perhaps best regarded as a warning that clarity of terminology is essential in medicine.

Finally, Marsden's data from a review article he wrote on hysteria has not been published elsewhere. It appears to refer to rates of misdiagnosis from referrals to his own movement disorders clinic, it is difficult to interpret as only basic figures are given but the impression is of a very highly selected population.

7.5. Health care utilisation.

Three studies gave information on the health care utilisation of MUS patients who present to neurology clinics (Hamilton *et al* 1996, Mace and Trimble 1996, Binzer and

Kullgren 1998). A fourth study Kirk and Saunders 1977 offers data on other previous consultations the subjects had made, but there was no indication of how the information was gathered. They do not appear to have either interviewed the subjects or consulted GP records. Their findings are therefore of questionable validity and impossible to interpret.

Hamilton *et al* estimated costs for the index consultation only. They showed that one quarter of patients (84/343) required no investigations whatsover (46 organic: 38 MUS). Of the remaining patients the costs of investigation were higher in the patients with organic diagnoses (median £89 compared with £41, $p<0.01$). Four percent of patients in this study were referred to psychiatrists and a further 2% started on antidepressants. In only 2% of patients was a specific symptomatic treatment recommended. More commonly, in one third of patients, general management strategies (e.g. start antispasmodic if pain recurs) were recommended. The commonest management (60%) was a statement to the GP that organic disease had been excluded without any further recommendations.

Mace and Trimble collected data on health care utilisation by direct interview with patients. They often extrapolated the findings from a "typical year" to provide ten year figures. They found that patients had a median (mean) of 55 (79.3) GP visits and 18 (33) specialist out-patient consultations, with 2.5 (2.8) different departments visited. Patients spent a median of 2 (11.6) weeks in general hospitals and 0 (1.5) weeks in

psychiatric hospital. They also had a median of 3.5 (47.7) other NHS consultations. Only a limited number of patients visited alternative practitioners (median 0, mean 5.4). The discrepancies between median and mean values demonstrates that resource utilisation is heavily skewed by a small number of patients who are very high consumers of resources.

Binzer and Kullgren offer limited data on health care utilisation demonstrating that patients who remained symptomatic had a mean of 6.7 GP visits per annum compared to 2.4 in those who remitted. The symptomatic patients also attended more out-patient consultations (mean, 4.7 compared to 1.0).

7.6 Do neurologists find patients with unexplained symptoms more difficult to help?

No studies were found which examined this question.

7.7. Discussion.

Medically unexplained symptoms are common in neurological practice with a likely prevalence somewhere between 20-40% of all presenting patients. Sampling techniques and definitions affect the quoted prevalence rates. All authors who examined the question found MUS to be associated with multiple symptoms, pain and higher rates of distress. There does not, to date, appear to have been a systematic examination of disability/health status in neurological MUS patients, although Creed *et al* and Ewald *et al* imply that disability was caused by the symptoms.

There was a paucity of outcome studies on MUS in neurology with only one study, from 1961, examining all MUS patients. The remaining studies concentrated specifically on patients with conversion hysteria. Nonetheless, it was clearly demonstrated that there was no evidence to support Slater's widely disseminated claim that the majority of patients diagnosed with conversion hysteria would eventually be shown to have organic neurological disease. The rate of misdiagnosis was around 5% in appropriately conducted studies. Of note, the study that examined all MUS patients found a similar rate of misdiagnosis to those that specifically examined the outcome of conversion hysteria. Only one study, Couprie *et al* systematically examined outcome using objective measures of disability but nonetheless the reported data makes it clear that where symptoms continued the associated functional disability could be high. Most studies reported findings that roughly half of patients remitted and the other half remained symptomatic. Short duration of symptoms and mood disorders appeared to be related to good prognoses. Conversely, personality disorder, financial benefits and compensation were associated with bad prognoses. Variables related to illness behaviour did not appear to affect outcome.

The evidence on health care utilisation was extremely limited. What data existed suggested that patients with conversion hysteria were probably high users of health care resources. However they also showed that, as in other health care situations, the distribution curve of utilisation was highly skewed with a small number of patients

being very high consumers of resources indeed. There were no studies examining neurologists' attitudes to patients with MUS.

Why have different studies shown different results? Clearly sources of patients samples were an important potential bias. There was a suggestion that the rate of misdiagnosis may be higher for patients seen at the National Hospital for Nervous Diseases, London. This could be down to the poor clinical skills of doctors working there, but a much more likely explanation was that they were examining a highly skewed sample of patients with an emphasis on diagnostic uncertainty. There was some suggestion that the diagnosis could be particularly difficult with patients suffering from unusual movement disorders. In addition patient ascertainment methods may have been important. Few of the outcome studies had genuine prospective methodologies and selection of patients was clearly dependent upon how their conditions were described and classified in the case notes. There is no way of knowing how many potentially eligible patients were excluded from samples via this potential bias. Likewise not all studies had a reproducible system for actually classifying what was meant by MUS or hysteria. This source of error was highlighted in the Slater study which enrolled many patients with organic disease and histrionic personality.

For the clinician there was little doubt that MUS do represent a clinical challenge in terms of diagnosis. The vast array of potential presentations reinforced Sydenham's claim that MUS were the "great chameleon of medicine". This is further backed up by

the bewildering array of individual case reports. There have been frequent reports of quadraplegia (Apple 1989, Baker and Silver 1987, David *et al* 1995), unconsciousness (Hopkins 1973), astasia abasia (Sinel and Eisenberg 1990), myoclonus (Walters *et al* 1988, Monday and Jankovic 1993), parkinsonism (Walters *et al* 1988), camptocormia (Miller and Forbes 1990, Sinel and Eisenberg 1990, Perez-Sales 1990), and pseudoptosis (Hop *et al* 1997). Whilst presentations of unexplained tremor (Kim et al 1999), gait disorders (Keane 1989), movement disorders (Factor *et al* 1995), blindness (Kathol *et al* 1983, Beatty 1999) seizures (Pakalanis *et al* 1991, Alper *et al* 1995, Lesser 1996, Bowman 1998) and headache (Packard 1980, Fitzpatrick and Hopkins 1981) are so common that large case series have been studied and diagnostic pointers described. Diagnosis is dependent on careful history taking and skilled clinical examination. The case reports demonstrate that, as a rule in the diagnosis of MUS, the role of clinical investigation is to exclude findings rather than to confirm them. The possible exception to this is non-epileptic seizures where video telemetry has a useful role in difficult to diagnose cases. Reports detailing misdiagnosis of MUS (Lang 1995, Miller 1988), as well as the outcome studies already cited, indicate that movement disorders, paralysis and stroke may be the most commonly misdiagnosed conditions. Errors appear particularly likely when patients with longstanding psychiatric complaints develop medical problems or when medical problems initially present with psychiatric complaints. However, heed should be paid to the warning given by Nimnuan *et al* (2000): when it comes to the misdiagnosis of MUS, it is the erroneous diagnosis of an 'organic' condition when the patient actually has MUS that is a far more common

source of clinical error. Further, it is an error that often has more, not less, serious consequences for the patient (Fink 1992).

In the description of MUS, use of the phrase 'organicity' or description of symptoms as 'non-organic' is of course deeply flawed. Unfortunately, such dualistic descriptions belong to a language doctors speak. Evidence is beginning to accrue that such symptoms may have an organic basis, linked with disordered physiological function. The associations with emotional disorders and psychological distress are not compromised by this assertion as few would seriously assert that such disorders are not also linked with altered brain function. Investigations have been made using numerous methodologies and amongst the most interesting findings are those studies using evoked potentials and functional imaging. The former has a longer history dating from a report by Hernandez–Peon *et al* (1963). This group reported clear-cut evoked activity from the normal arm of a patient, but no substantial evoked activity with stimulation of the anaesthetic arm. However, there were conflicting reports from other groups who failed to replicate this finding (Bergami and Bergamasco 1967, Halliday 1968). Levy and Mushin (1973) attempted to clarify the situation and reported that if a nerve electrical stimulation technique was used, near threshold responses from the anaesthetic area were significantly smaller than the normal arm, but with higher levels of stimulation there was no appreciable difference. By contrast, if a skin electrical stimulation technique was used, the anaesthetic area evoked a consistently smaller response irrespective of whether the stimulus was near threshold or supra-maximal. Using a different technique,

Moldofsky and England (1975) were surprised to find a more complex pattern of inhibition and facilitation, which they linked to Lader and Sartorius' (1968) findings of slower habituation of galvanic skin response in hysterical patients. A more sophisticated approach was used by Lorenz *et al* (1998) who introduced an odd-ball paradigm into testing of anaesthetic limbs. They demonstrated an absence of a P300 component when the paradigm was tested on the 'hysterical' limb but not in the ordinary limb or in the limbs of a control subjects feigning anaesthesia.

Studies using functional imaging techniques have offered novel methods for examining the basis of hysterical symptoms. Marshall *et al* (1997) reported on a woman with hysterical paralysis of her left leg. Attempts to move the leg failed to activate the right primary motor cortex, and instead, activated the right orbito-frontal and right cingulate cortex. They suggested that these areas inhibited prefrontal, willed, effects on the right primary motor cortex. Halligan (2000), from the same group, went on to replicate this finding in subjects with hypnotically induced paralysis. Yazici and Kostakoglu (1998) found evidence of change of blood flow, with markedly reduced perfusion in temporal lobes, in a study of five patients with hysterical gait disorders imaged with [^{99m}Tc]HMPAO SPECT scans. Tiihonen *et al* (1995) showed hypoperfusion of the right parietal lobe, in a case of left sided hysterical paraesthesia, scanned during median nerve electrical stimulation. The changes resolved following resolution of the symptoms. The study of phantom limb pain (Ramachandran and Ramachandran 2000) has also led to suggestions of neural plasticity within body sensory maps which can

change over time and lead to altered conscious experiences. Whilst these findings are individually interesting it would certainly be erroneous to think that researchers were in anyway close to having a comprehensive explanation for MUS. Or indeed that experimental error could not explain the entirety of the abnormal findings to date. However, taken in conjunction with the abnormal findings from other MUS syndromes such as chronic fatigue and irritable bowel (see previous chapter) there is a strong suggestion that disorders of functional physiology may be of aetiological importance.

In summary this systematic review found evidence that medically unexplained symptoms account for approximately one third of neurological practice. There was some evidence suggesting that MUS caused functional disability to patients but there was a lack of systematic examination of this. There was a clear association between the presence of MUS and increased rates of anxiety and depression. The diagnosis of MUS was accurate in approximately 95% of cases. There was virtually no outcome data on MUS in neurology but studies conducted on patients with conversion disorder suggested that approximately half will remain symptomatic. Some, but not all, patients with MUS are high consumers of health care resources. There is no data on whether neurologists find MUS patients difficult to help.

Chapter 8. Do medically unexplained symptoms matter?

8.1 Introduction.

The literature reviews have demonstrated that patients who present with symptoms that are unexplained by organic disease are common in all medical settings. There is however much less information on, and acceptance of their importance as a clinical problem, however. This chapter describes the cross sectional results of a study conducted in a neurological service to determine the prevalence of such patients and their importance as defined by patients' disability and distress. The methodolgy of the study is outlined in chapter 3.

8.2. Aims.

Primary Aim:

To determine the proportion of patients newly referred to general neurology outpatient clinics who have medically unexplained symptoms.

Secondary Aims:

i. To determine the validity of the initial diagnosis of medically unexplained symptoms in terms of whether unexpected *organic* causes were discovered by time of six month follow-up.

ii. To determine why patients with medically unexplained symptoms were referred to the neurology out-patient clinic.

iii. To determine the health status of patients with medically unexplained symptoms and compare it to patients whose symptoms were explained by *organic* neurological disease.

8.3. Analysis and justification of statistical techniques.

Analysis strategy:

The analysis was undertaken in three stages:

The prevalence of medically unexplained symptoms (MUS) was calculated from the neurologists *organicity* rating.

The GP's reason for referral was examined by *organicity* rating.

The four groups defined by the neurologists' *organicity* rating were compared for health status, number of physical symptoms and emotional disorder diagnoses. The non-parametric Kruskal-Wallis test was employed as the data were not normally distributed. Confidence intervals were calculated using non-parametric techniques and appropriate tables (Gardner and Altman 1989).

Justification of Statistical Techniques:

The standard level of significance of $p<0.05$ was used to reject the null hypothesis. Although all tested hypotheses had predicted directions, as detailed in the literature reviews, two tailed tests of significance were used throughout the analysis. It was not appropriate to correct for multiple testing using a Bonferroni technique or similar as there was no universal null hypothesis only individually tested hypotheses (Perneger 1998).

Non-parametric tests do not require assumptions about underlying distributions. Within this context the Kruskal-Wallis test will test whether two or more independent samples (in this case the four organicity groups) come from the same population. It is a non-parametric equivalent of a one way analysis of variance and is based upon an extension of the Mann-Whitney U test. There is no assumption of ordering within the populations from which the samples are drawn but there is an assumption that samples tested will be similar in shape. The test, like the Mann Whitney, runs on the assumption that if results from the two or more independent samples are combined and ranked and then the number of times a score from group 1 precedes a score from group 2 should be randomly distributed. The test statistic H is calculated from comparisons of ranking position, it follows the chi squared distribution. As the comparison depends upon position of a variable within the sample the median not the mean is the appropriate summary statistic. A statistically significant result means that the hypothesis that the groups come from populations with the same median is rejected (Altman 1991).

Confidence intervals are shown, in addition to P values, as they demonstrate the degree of uncertainty, or lack of precision, of the estimate of interest (Altman 1991).

8.4. Results.

Of 364 new patients booked in the designated clinics during the study period 48 did not attend, leaving 316 eligible to participate. Of these, 12 refused, one was too cognitively impaired to be assessed, two patients were lost to assessment, and

one found the assessment distressing and withdrew. This left 300 patients, a participation rate of 96% of attenders and 82% of referrals.

Of the patients included 174 (58%) were female. The mean age was 43 (range 14 to 88) years. Table 8.1 describes the neurologists' final *diagnoses* of patients in the sample. In some cases the *diagnoses* were merely symptom descriptions. Of the 300 patients 33 (11%) had symptoms which were considered to be *not at all explained* by organic disease and a further 57 (19%) had symptoms only *somewhat explained* by organic disease. This compared to 81 (27%) who had symptoms *largely explained* and 129 (43%) whose symptoms were *completely explained* by organic disease. At six-month case note review, there had been little change of the neurologists' opinion concerning *organicity*. In four cases expected organic causes were not confirmed by investigation. In a further six cases, where subjects had been rated as having *largely* or *completely* explained symptoms, unexpected *organic* causes of disease were found. Thus, although the diagnosis changed the *organicity* rating did not. There were no cases in which an *organic* cause emerged for symptoms initially considered *not at all* or *somewhat* explained.

The GPs' reason for referral is shown in table 8.2. When the reasons for referral were compared by *organicity* rating we found that approximately two thirds (14, 64%) of the 22 patients who had been referred at their own request had symptoms that were *largely* or *completely* explained by *organic* disease. Of those 28 patients referred *to reinforce my opinion of no neurological disease* 11 (39%) were

Table 8.1. **Diagnoses given to illustrate case mix n=300[1]**

Diagnosis	N (%)
Headache	63 (21%)
Epilepsy/fits/pseudoseizures	43 (14%)
Multiple sclerosis	30 (10%)
Neuropathies (peripheral/ entrapment)	25 (8%)
Syncope	22 (7%)
Spinal pathology (cervical/lumbar)	22 (7%)
'dizziness'	8 (3%)
Parkinson's disease	7 (2%)
Psychiatric diagnosis only	7 (2%)
Other [2]	73 (26%)

1- Diagnoses do not necessarily indicate neurological disease; some are merely symptoms descriptions.

2- Diagnoses in the 'other' category each had a frequency of less than 2%.

Table 8.2. **General Practitioners' stated principal reason for referral.**

	Number of referrals (%) (n=300)
Diagnosis and treatment	155 (52)
Patient request	22 (7)
Reinforce my opinion no disease	28 (9)
Other [1]	37 (12)
Referred by GP Trainee [2]	9 (3)
Referred by other consultant	24 (8)
No response from GP	25 (8)

1- In most cases this was to seek advice on use of a specific medication, e.g. β interferon, or anti-convulsants during pregnancy.

2- GP trainees were no longer with the practices and their reason for referral is unknown.

considered by the neurologists to have symptoms which were *largely* or *completely* explained.

Patients' characteristics are shown in table 8.3. The groups did not differ substantially or significantly in terms of age or sex. Neither, were there statistically significant differences between them in their general health perception, physical function or physical role function as measured by the SF-36. Patients whose symptoms had lower *organicity* ratings did however report a significantly greater number of physical symptoms, more bodily pain and more impaired social functioning. A significantly greater number of patients in the low *organicity* groups were diagnosed as suffering from anxiety and depressive disorders. This was reflected in their increased impairment on the vitality, emotional role function, and mental health scales of the SF-36.

8.5. Discussion.

One third of new general neurology outpatient attenders had symptoms which were either "not at all" or only "somewhat" explained by organic disease. A six-month case note review showed that further assessment and investigation had not revealed an "organic" cause of disease in any of these patients. In the few cases where opinion did change, this was only because expected "organic" causes of disease were not confirmed by further assessment and investigations. The neurologists' ratings of medically unexplained symptoms were therefore valid, at least in the short term.

Table 8.3. **Associations of the neurologists' 'organicity' rating of patients' symptoms with age, sex, disability and emotional disorders.**

Variable	To what extent can the patient's symptoms be explained by organic disease?					
	Not at all	Somewhat	Largely	Completely	Chi Square (3df)	P value
Number of patients (%)	33 (11%, 7% to 14%)	57 (19%, 15% to 23%)	81 (27%, 22% to 32%)	129 (43%, 37% to 49%)		
Number male (%)	11 (33%, 18% to 52%)	22 (39%, 26% to 52%)	34 (42%, 31% to 53%)	58 (45%, 36% to 54%)	1.9	0.6
Median age	40 (37 to 44)	41 (37 to 43)	40 (36 to 44)	43 (40 to 48)	1.9	0.6
Median no. of physical symptoms	6 (4 to 8)	5 (4 to 6)	5 (4 to 6)	3 (2 to 3)	35.3	<0.0005
Median SF-36 scores[1]						
General health	57 (52 to 60)	57 (57 to 60)	57 (52 to 57)	57 (55 to 57)	1.4	0.7
Physical functioning	75 (70 to 90)	85 (65 to 95)	85 (70 to 95)	80 (75 to 85)	0.4	0.9
Role functioning -physical	50 (0 to 100)	50 (25 to 100)	75 (50 to 100)	75 (75 to 100)	2.9	0.4
Bodily pain	51 (31 to 64)	51 (40 to 60)	61 (50 to 70)	74 (72 to 84)	21.1	<0.0005
Social functioning	62 (50 to 100)	62 (50 to 75)	75 (62 to 100)	88 (88 to 100)	16.3	0.001
Vitality	40 (30 to 45)	45 (35 to 50)	50 (40 to 55)	50 (50 to 60)	16.3	0.001
Role functioning -emotional	100 (0 to 100)	67 (0 to 100)	100 (0 to 100)	100 (100 to 100)	18.4	<0.0005
Mental health	56 (48 to 68)	60 (52 to 68)	72 (64 to 76)	76 (72 to 80)	21.3	<0.0005
No. (%) with anxiety or depressive disorder	23 (70%, 51% to 84%)	37 (65%, 51% to 77%)	39 (48%, 37% to 60%)	41 (32%, 24% to 40%)	26.2	<0.0005

Note- all confidence intervals, in brackets, 95% approx.
1- all SF 36 scores range from 0 to 100, a lower score equates with *poorer* health status.

In the majority of cases, patients with unexplained symptoms had been referred because they "needed neurological diagnosis and possible treatment". Given this, and the finding that 39 % of the patients referred to "reinforce my opinion of no neurological disease" in fact had definable organic disease, one can conclude that specialist opinion has an important role to play in clarifying the clinical situation in these complex patients.

Self-reported physical functioning was just as impaired in patients whose symptoms were of lower 'organicity' as in those whose were associated with identified 'organic' disease. Furthermore, patients with complaints of low 'organicity' reported a greater number of physical symptoms, more pain, and were more likely to have emotional disorders. Symptom clusters of multiple, painful complaints, particularly in depressed or anxious patients, should be regarded as diagnostic pointers towards unexplained symptoms. It should be noted that this is a highly debilitating picture and comments such as "don't worry, there is nothing really wrong here" are likely to be disbelieved or annoy patients who perceive themselves to be in great suffering. Therefore, clinically it is necessary to give some validation to the reality of the patients' symptoms before starting to explore aetiological models with them.

These findings must be considered in the context of potential methodological shortcomings: First, although the clinics were considered representative of the overall service, and referrals were taken from a common pool, certain specialized clinics, in particular neurovascular and memory clinics, were not represented in

the study sample. The sample may therefore not be fully representative of neurology outpatient referrals. This limitation notwithstanding, the very high participation rate of 96% of patients suggests that this sample is representative of new attenders to the general neurology outpatient clinics. Second, there must be some uncertainty about how the threshold for referral, or the view of what constitutes an appropriate referral among local GPs, compares with that of GPs elsewhere.

The finding that 30% of referred patients had symptoms that were not well explained by organic disease is in agreement with previous reports. Perkin (1989) in his review of 7836 consecutive new neurological patients whom he had seen personally at Charing Cross Hospital reported that 26% of patients received no medical diagnosis, and a further 4% had symptoms of conversion hysteria. Similar findings have been shown in female in-patient neurological populations by Creed *et al* (1990). The important new findings described in this thesis are that this group of patients are disabled by their symptoms and suffer from very high rates of emotional disorder.

This frequency of medically unexplained symptoms does not appear to be unique to general neurology. Two retrospective case note reviews indicate the frequency in other settings: in US ambulatory care Kroenke and Mangelsdorff (1989) found that only 16% of physical complaints were explained by organic disease. In UK outpatient care, Hamilton *et al* (1996) reported rates of 53%, 42% and 32%, in

gastroenterology, neurology and cardiology, respectively, for the percentage of patients whose symptoms remained medically unexplained after assessment.

In this study, the patients with anxiety and depressive disorders were over-represented among those whose symptoms were considered less "organic". However, it should be noted both that emotional disorders were also common in patients with identifiable neurological disease and that many of the patients with unexplained symptoms did not have definite evidence of emotional disorder.

Given the substantial number of patients with symptoms largely unexplained by identifiable 'organic' disease; disability at least as high as in those patients with a more definite explanation for their symptoms and a greater likelihood of emotional disorder, one can conclude that medically unexplained symptoms do matter.

Chapter 9. Depression, anxiety and health status: are they related?

9.1 Introduction.

The previous chapter demonstrated that medically unexplained symptoms were common, disabling and associated with an excess of anxiety and depressive (emotional) disorders. In this chapter the association between these emotional disorders and patients disability shall be examined.

Hospital medical services have traditionally been organised into distinct medical/surgical and psychiatric services. The medical/ surgical sector offers treatment for 'organic diseases' and the psychiatric for 'psychiatric illness'. However, the literature reviews and the previous chapter have demonstrated the limitations of this and there is increasing evidence that many patients would benefit from a combined approach (RCP and RCPsych 1995).

Only a few studies have examined psychiatric disorders in medical out-patients (see chapters 6 and 7). These suggest that depression and anxiety disorders are not only common but may contribute to patient disability. The systematic review demonstrated that although several studies had examined cross sectional prevalence rates in neurology outpatient clinics, no study had examined the potential association between emotional disorders and disability, nor had they examined specifically for rates of suicidal ideation.

9.2. Aims.

Primary aim:

To determine the prevalence of anxiety and depressive (emotional) disorders among new attenders at general neurology outpatient clinics.

Secondary aims:

i. To determine the association between emotional disorders and health status.

ii. To determine whether the association between disability and health status was affected by whether the patient has medically unexplained symptoms or *organic* neurological disease.

iii. To determine the rate of suicidal ideation among new attenders at general neurology out-patient clinics.

iv. To determine the rate of depressive disorders among patients with significant suicidal ideation.

v. To determine whether significant suicidal ideation was related to the presence of medically unexplained symptoms or to *organic* neurological disease.

9.3. Analysis and justification of statistical techniques.

Analysis strategy:

The HAD was scored to produce both separate depression and anxiety ratings and also a total *emotional distress* score .The PRIME MD was used to generate individual DSM-IV diagnoses. All anxiety and depressive diagnoses were then combined to produce a category of emotional disorder used in further analysis.

The SF-36 scale scales were converted to percentages as recommended by the authors. In all domains of the SF-36 a lower functioning score indicates increased disability/pain.

Associations between emotional disorders and disability were examined as follows: first, the correlations between the continuous scale of severity of distress (HAD) and SF-36 scores were examined. Second, the SF-36 sub-scale scores of those with a diagnosis of emotional disorder and those without were compared. Then, to test the hypothesis that any association between emotional disorder and disability was due to neurological disease the two subsamples described above (those with a diagnosis of emotional disorder and those without) were further divided according to the presence or absence of neurological disease. This distinction was made by dichotomising the final scores from the neurologists' *organicity* rating into *neurological disease* (*largely explained* and *completely explained*) and *medically unexplained symptoms* (*not at all explained* and *somewhat explained*). A comparison of disability ratings across the four groups was then made. The data were not normally distributed so the Kruskal Wallis test was used. Confidence intervals were calculated using non-parametric techniques and tables (Gardner and Altman 1989).

The number of somatic symptoms reported by the patient was analysed in a similar fashion.

In order to have a detailed examination of suicidal ideation the prevalence of significant suicidal ideation was calculated. Then the association between suicidal

ideation and the presence of depressive disorder was examined. Finally, suicidal ideation was examined by the presence or absence of *medically unexplained symptoms* (as above). To aid interpretation those with *neurological disease* were further dichotomized into those disorders which were *potentially progressive* (e.g. multiple sclerosis, Parkinson's disease, brain tumours) and those which were *non-progressive* (e.g. epilepsy, headache, migraine, neuropathies).

Justification of Statistical Tests:

Correlations between HAD score and SF-36 scores were conducted using the Spearman's Rank Correlation test. This is a non-parametric test of the association between two numerical variables. As such, no prior assumptions about distribution shape are made. The test is conducted by independently ranking the values of each variable and the measure (r) is based upon the differences between the pairs of ranks of the two variables. Two aspects of correlation should be noted. Firstly, a correlation does not necessarily imply a 'cause and effect' relationship. Secondly, the significance level of a correlation is both a function of the size of the correlation co-efficient and the number of observations. Thus in this study a significant correlation is expected but it is the strength of the correlation that is of interest and will be reported. An aid to interpretation of correlations scores can be made by from the formula $100r^2$ which calculates the percentage of the variability between the two variables that can be explained by the association. Thus r=0.7 explains 49% of the variability, r=0.5 explains 25% of the variability, and r=0.3 only 9% of the variability (Altman 1991).

The Kruskall-Wallis test has been outlined in the previous section. As noted a significant result from a Kruskall-Wallis test does not explain which *particular* independent sample was not from the same population. In this section of the analysis the related Mann Whitney test has been used to confirm which sample did indeed differ (Altman 1991).

To examine suicidal ideation in more detail the relative risk statistic was calculated. Relative risks allows comparison of two groups with respect to risk of some event. It is calculated from a two by two table when there are two groups of subjects and only two types of outcome. It is properly used in prospective cohort studies (the odds ratio being the measure of choice for retrospective case-control studies). The proportion having the outcome in each group is calculated and expressed as a ratio. Thus under the null hypothesis the risk is one. Confidence intervals can be calculated from the standard error of the logarithm of the relative risk (Altman 1991).

9.4. Results.

The median HAD total score for the sample was 10, with a median HAD depression score of three and anxiety score of six. Criteria for one or more DSMIV diagnoses of emotional disorder were met by 140 (47%) of patients (Table 9.1). 67 patients met criteria for more than one disorder, in 58 cases this was major depression plus another disorder.

Table 9.1. **Psychiatric diagnoses showing number of patients (and percentage) in each diagnostic category (n=300)[1].**

DSM IV Diagnosis	Number (%, 95% C.I.)
Major Depressive Disorder	77 (26%, 21% to 31%)
Minor Depressive Disorder[2]	23 (8%, 5% to 11%)
Dysthymia	46 (15%, 11% to 19%)
Panic Disorder	21 (7%, 4% to 10%)
Generalised Anxiety Disorder	28 (9%, 6% to 13%)
Anxiety Disorder NOS[3]	53 (18%, 13% to 22%)

1- 67 (22%) patients met criteria for more than one disorder
2- Minor depression was diagnosed according to DSM IV research criteria
3- Not Otherwise Specified

Table 9.2 shows correlations between the HAD scores (*emotional distress*) and the SF 36 scores (disability). It can be seen that the HAD depression score was more closely associated with disability, particularly in physical function and role functioning-physical domains, than the HAD anxiety score.

The main finding was that patients with emotional disorders were substantially more disabled on all eight subscales of the SF 36 (Table 9.3). (Four of the subscales of the SF-36, general health perceptions, vitality, emotional role functioning and mental health, measure symptoms that substantively overlap with those recorded by the PRIME-MD and the HAD scale. No further comment is made on scores from these four subscales as they add no meaningful data). Furthermore, subdivision of the sample into those with neurological disease, 210 (70%), and those with unexplained symptoms, 90 (30%) (see Table 9.4) indicated that this association with emotional disorder was *independent* of the presence of *neurological disease*.

An analysis of the associations between emotional disorder and number of somatic symptoms revealed that patients with an emotional disorder reported twice as many somatic symptoms as patients without an emotional disorder. Again, independent of the presence of neurological disease (Tables 9.3 and 9.4).

The associations between individual emotional disorder diagnoses and disability were not examined for two reasons. Firstly, there would be small numbers in

Table 9.2. **The correlations between scores on the Hospital Anxiety and Depression Scale and scores on theSF-36 sub-scales and the reported number of somatic symptoms (n=300).**

		SF 36						
	No. of somatic symptoms	**physical function**	**physical role function**	**bodily pain**	**social function**	**HAD total score**	**HAD depression score**	**HAD anxiety score**
HAD total score	0.5	-0.3	-0.4	-0.4	-0.6	-	0.8	0.9
HAD depression score	0.4	-0.5	-0.4	-0.4	-0.5	0.8	-	0.6
HAD anxiety score	0.4	-0.2	-0.2	-0.3	-0.4	0.9	0.6	-

All the correlations were statistically significant ($p<0.0005$, 2 tailed)
In the SF36 lower scores indicate increased disability or pain, hence the negative correlations between HAD and SF36 scores.

Table 9.3. **Relationship between emotional disorder, demographics, HAD score, disability, pain, and the number of somatic symptoms. (n=300)**

	Emotional Disorder n=140	No Emotional Disorder n=160	Mann Whitney U	p
Number male	50 (36%, 28% to 44%)	76 (48%, 40% to 55%)	4.3[a]	0.04
Median age	41 (38 to 44)	42 (38 to 44)	10670	0.7
Median total HAD score	17 (14 to 19)	6 (6 to 8)	2374	<0.0005
Median SF36 Score[b]				
Physical function	70 (60 to 80)	90 (90 to 95)	7431	<0.0005
Physical role functioning	25 (0 to 50)	100 (75 to 100)	6658	<0.0005
Bodily pain	51 (42 to 52)	80 (72 to 84)	5115	<0.0005
Social functioning	62.5 (50 to 62.5)	100 (100 to 100)	6914	<0.0005
Median no. somatic symptoms	6 (5 to 7)	3 (2 to 3)	5104	<0.0005

(a) Chi square test
(b) Lower scores on the SF36 equate with increased disability or pain; all scores range 0-100
All (x to y)- confidence intervals at 95% approx.

Table 9.4. **Relationship between emotional disorder, demographics, total HAD score, disability, pain and somatic symptoms showing the effect of subdividing the sample according to the presence or absence of "organic" neurological disease (N=300)**

	Emotional disorder		No emotional disorder			
	Unexplained symptoms n=60	**Neurological disease** n=80	**Unexplained symptoms** n=30	**Neurological disease** n=130	Chi square[3]	p
number male (%)	23 (38%, 26% to 52%)	27 (34%, 24% to 45%)	10 (33%, 17% to 53%)	66 (51%, 42% to 59%)	7.2	0.07
median age	38 (36 to 41)	43 (40 to 51)	43 (38 to 47)	40 (37 to 44)	3.7	0.3
Median total HAD score	17.5 (14 to 19)	16 (12 to 20)	7.5 (4 to 10)	6 (5 to 7)	140	<0.0005
median scores SF 36[4]						
physical function	72.5 (65 to 85)[1]	60 (50 to 70)[1]	90 (75 to 100)[2]	90 (85 to 95)[2]	27.8	<0.0005
physical role functioning	25 (0 to 50)[1]	25 (0 to 50)[1]	100 (75 to 100)[2]	100 (75 to 100)[2]	41.2	<0.0005
bodily pain	41 (30 to 50)[1]	52 (40 to 60)[1]	68 (52 to 84)[2]	84 (72 to 84)[2]	37.5	<0.0005
social function	50 (37.5 to 62.5)[1]	62.5 (50 to 75)[1]	100 (62.5 to 100)[2]	100 (100 to 100)[2]	72.3	<0.0005
median no. somatic symptoms	6 (5 to 7)[1]	6 (5 to 6)[1]	3 (2 to 5)[2]	3 (2 to 3)[2]	70.2	<0.0005

1- Between group comparisons using Mann Whitney U test all non significant (p>0.05)
2- Between group comparisons using Mann Whitney U test all non significant (p>0.05)
3- Kruskall Wallis test, 3 degrees freedom
4- A lower score on the SF 36 equates with increased disability: all subscales range from 0-100.
All (x to y)- confidence intervals at 95% approx (non-parametric).

individual cells increasing the likelihood of errors. Secondly, about one third of patients with emotional disorders had more than one diagnosis.

Twenty six out of 300 patients (9%, 95% C.I. 6% to 12%) reported significant suicidal ideation in the two weeks prior to their initial attendance at neurology out-patients (table 9.5). Almost all of these patients (23/26) were suffering from major depressive disorder. Twelve of the 26 patients had *medically unexplained symptoms* (RR 1.62, 95% C.I. 1.03 to 2.56). Only two of them had *potentially progressive neurological disease*.

9.5. Discussion.

Almost half of new attenders at neurology clinics in Edinburgh had an emotional (anxiety or depressive) disorder. The most common diagnostic category was major depression (26%). These emotional disorders were strongly associated with increased disability, more pain, more somatic symptoms. This association was present whether analysed using a continuous variable (the HAD score) or a categorical approach (the PRIME-MD produced DSM IV diagnoses). On the HAD scale the relationship was strongest for depressive symptoms. The association of disability and emotional disorder was equally strong in those with unexplained symptoms as those with neurological disease.

Furthermore, one in eleven patients (26/300) seen at general neurology outpatient clinics had given serious thought to committing suicide in the last two weeks. Almost all of these patients (23/26) were suffering from major depression. It

Table 9.5. **Clinical characteristics of 300 consecutive new attenders at neurology out patient clinics dichotomised by the presence or absence of significant suicidal ideation.**

	suicidal ideation, n (%) n=26	no suicidal ideation, n (%) n=274	Relative Risk (95% C.I.)
Male	12 (46%)	114 (42%)	1.11 (0.71 to 1.72)
Female	14 (54%)	160 (58%)	0.84 (0.40 to 1.76)
Aged forty years or under	15 (58%)	128 (47%)	1.50 (0.71 to 3.15)
Major depressive disorder	23 (88%)	54 (20%)	4.49 (3.40 to 5.92)
Medically unexplained symptoms	12 (46%)	78 (28%)	1.62 (1.03 to 2.56)
Non-progressive neurological disease[1]	12 (46%)	153 (56%)	0.83 (0.54 to 1.27)
Potentially progressive neurological disease[2]	2 (8%)	43 (16%)	0.49 (0.13 to 1.91)

1- includes conditions such as epilepsy, headache, migraine, neuropathies
2- includes conditions such as multiple sclerosis, Parkinson's disease, brain tumours
3- identified as needing psychiatric or psychological assessment and/or treatment; not specifically as being suicidal.

might be assumed that suicidal ideation would more likely occur in those suffering from progressive, debilitating neurological conditions. However, this was not the case. Twelve of the 26 suicidal patients had medically unexplained symptoms and the most of the remainder had non-progressive conditions. This finding does not support the idea that suicidal ideation in neurology patients is largely a rational response to progressive physical illness. Instead, it underscores the importance of major depressive disorder in influencing the ways "medical" patients think about their illnesses and themselves.

When interpreting results one must consider the representativeness of the sample. The participating clinics were representative of the overall service and referrals were taken from a common pool. However certain specialised clinics, in particular neurovascular and memory clinics, are not included and potentially render our sample unrepresentative of patients seen in less specialised services. Nonetheless, the very high participation rate (96%) indicated that this sample is representative of new attenders to the Edinburgh general neurology clinics.

The PRIME-MD is based on the Structured Clinical Interview for DSM III-R (Spitzer *et al* 1992) and has been tested extensively in four American primary care settings (Spitzer *et al* 1994), three of which were hospital based clinics and one was a family based clinic. The overwhelming majority of patients in the original sampling frame had a co-morbid physical disorder. In this patient group it was specific for the major diagnostic categories; 92% for any mood disorder, 98% for major depression, 96% for dysthymia, 99% for panic disorder and 97% for

generalized anxiety disorder. Its weakness was sensitivity, with a detection rate of 67% for any mood disorder and 83% for any psychiatric condition . In this study an attempt was made to improve the sensitivity by asking all the questions from each module in the interview schedule, as it had been originally designed, and omitted the screening questionnaire that was later developed to decrease the time spent in completing the interview. If it remained insensitive, this will have resulted in an underestimate of psychiatric morbidity. An examination of the difference in median total HAD scores, in this sample, between those identified by the PRIME MD as having an emotional disorder (median 17) and those who don't (median 6), demonstrates a difference of 11 points, providing further reassurance of the validity of the PRIME MD in patients with co-morbid physical illness.

In accordance with the authors instructions the raw SF 36 scores were converted into percentages. It should be noted that although making the findings easier to interpret, this conversion can give the appearance that some domains, particularly the role functioning domains, have a greater range of scores than they actually do. For example, in the physical role functioning domain, the raw scores range from 4 to 8, and converted they range from 0 to 100.

One may ask whether the emotional disorders identified persist. Follow-up studies of in-patient populations have found that such disorders often remit following discharge (Mayou and Hawton 1986). The suggested explanation is that the emotional disorder reflects the stress of hospitalisation. This hypothesis may be less applicable to out-patients.

There have been only four previous studies of anxiety and depression in neurology outpatient clinics, one in the North-East of England (Kirk and Saunders 1977), two in the United States (Berlin *et al* 1983, Schiffer 1983) and one in the Netherlands (Van Hemert *et al* 1993). Two (Kirk and Saunders 1977, Berlin *et al* 1983) were carried out using self rating scales, the General Health Questionnaire (Goldberg 1972), and the Symptom Check List-90 (Derogatis 1977). In these studies the prevalence of patients with emotional disorder was 27% and 51% respectively. Neither scale allowed for the generation of individual diagnoses, but were limited to the use of cut-offs to describe a patient as "likely" to have a emotional disorder. The Dutch study used a diagnostic interview, the Present State Examination (PSE; Wing *et al* 1974), and found that 25% of new patients met PSE criteria for an emotional diagnosis, with depressive disorders (15%) being most common. The final study (Schiffer 1983) relied on the clinical impression of a neurology resident and reports a much lower rate of depression. None of these studies commented on disability or the perception of treatment need.

The results from this study are of particular interest because they demonstrated a strong relationship between emotional disorders and disability. In Wells *et al*s' study (1989), they also found that the combined presence of depression and a medical condition had a magnified effect on disability. Our findings replicate this in patients with neurological diseases, a group not included in Wells *et als*' study. Of particular interest is that the same effect exists in patients with unexplained symptoms.

The prevalence of 9% (95% confidence interval 6% to 12%) for significant suicidal ideation described in this study appears higher than the 2 –3% described in primary care and community settings in the USA.(Olfson *et al* 1996, Cooper-Patrick *et al* 1994, Zimmerman *et al* 1995, Paykel *et al* 1974). There is no data to indicate what proportion of the medically ill who report such suicidal ideation actually go on to kill themselves. Nonetheless, suicidal ideation of the type considered significant in this study is clinically significant in that it would be taken very seriously during a psychiatric consultation.

The previous chapter demonstrated that a two thirds of patients with medically unexplained symptoms had anxiety or depressive disorders. In this chapter it has been demonstrated that such disorders are associated with increased disability, poorer health status and more somatic symptoms. Furthermore, the combination of emotional disorder and unexplained symptoms was significantly associated with serious suicidal ideation. What should be done? The important questions now are first, do these emotional disorders persist? Second, does remission of an emotional disorder lead to reduction in the patient's disability? These questions will be examined in chapter 11.

Chapter 10. The outcome of patients with medically unexplained symptoms in neurology.

10.1. Introduction.

Chapter 8 demonstrated that 30% of new referrals to general neurological out-patient clinics had symptoms which were rated by the assessing neurologist as *not at all* or only *somewhat* medically explained. These patients were as disabled as those with identified neurological disease. In addition they reported higher rates of depression and anxiety disorders. However, there is little available data on the prognosis of such patients.

The systematic review demonstrated that has been few prospective studies of the prognosis of medically unexplained symptoms in neurology. Although there have been several reports of patients specifically diagnosed as having conversion disorder, these represent only a small proportion of patients attending neurological clinics with MUS. The systematic review found only one previous study, (Jacobs and Russell 1961), which included patients with a range of MUS. It was limited in scope and concentrated on the potential development of unexpected neurological explanations for the patients' symptoms rather than patient outcome in terms of symptoms and health status.

This chapter describes the results of follow up examination of the 90 patients with symptoms which were *not at all* or *somewhat* medically explained (chapter 8).

10.2. Aims.

Primary aim:

To determine the outcome of newly referred neurological out-patients with symptoms which were *not at all* or *somewhat* medically explained at eight months follow-up in terms of clinical global improvement.

Secondary Aims:

I. To determine the outcome of newly referred neurological out-patients with symptoms which were *not at all* or *somewhat* medically explained at eight months follow-up in terms of change in health status and the presence of psychiatric diagnosis at outcome.

10.3. Analysis and justification of statistical techniques.

Analyses strategy:

This section of results examined only those subjects who were rated as having symptoms which were *not at all* or *somewhat* medically explained (n=90) at initial assessment.

First a comparison was made of the results at initial assessment between those who participated in follow-up and those who did not in order to assess the possibility of systematic bias in the follow-up sample. Second, the clinical global improvement of patients was described. Third, the sample was dichotomised into those who were the same or worse and those who improved. The two groups were then compared in terms of age, sex, changes in health status, and presence of psychiatric diagnoses at outcome.

10.4. Results.

Of the 90 patients with symptoms which were *not at all* or *somewhat* medically explained at initial assessment, 66 (73%) participated in the follow-up assessment. The mean age of those who participated was 42, 62% were female. There were no substantive or statistically significant differences between those subjects that did and did not participate (table 10.1).

The clinical global improvement scores are described in table 10.2. It can be seen that 36/66 (54%, 42% to 67%) remained the same or got worse compared to 30/66 (46%, 33% to 58%) who improved. There were no differences in age and sex between those who improved and those who did not. Those who rated themselves as improved also reported significantly greater improvement in SF-36 scores and significantly fewer anxiety or depressive disorders at follow up (table 10.3).

Review of the neurological case records was complete for all 90 patients. It revealed that there were no cases where further assessment or investigation had uncovered an organic disease as an explanation for the presenting complaint.

Review of the primary care records was only possible for 58/66 patients who participated in follow-up. In three cases the patients gave consent for follow up only but did not wish their general practice case records to be reviewed. In the other five cases the general practitioners refused permission to access the case

Table 10.1. **Comparison of those followed up with those not followed up according to baseline characteristics.**

	Followed up	Not followed up	p
Number	66	24	
Mean age	42	39	0.36[1]
Number male	24 (38%)	9 (36%)	0.9[2]
No. with emotional disorder	44 (67%)	16 (67%)	1[2]

1- difference in means

2- chi square test.

Table 10.2. **The eight month self-rated clinical global improvement(n=66).**

Clinical Global Improvement	N (%, 95% CI)
Much worse	5 (8%, 3% to 17%)
Somewhat worse	4 (6%, 2% to 15%)
Just the same	27 (41%, 29% to 54%)
Somewhat better	15 (23%, 13% to 35%)
Much better	15 (23%, 13% to 35%)

Table 10.3.**The eight month outcome in health status between baseline and follow-up. This is shown by change in global clinical improvement dichotomised into 'same or worse' or 'improved' (n=66).**

	Same or worse	Improved	p
Number	36 (55%, 42% to 67%)	30 (45%, 33% to 58%)	
Mean age	43 (39 to 47)	39 (35 to 43)	0.4[a]
No.male	11 (31%, 16% to 48%)	13 (43%, 26% to 63%)	0.31[b]
Mean change in Sf-36 score			
Change in physical function	-9 (-14 to –8)	7 (2 to 12)	<0.0005[a]
Change in physical role func.	-8 (-21 to 6)	34 (20 to 48)	<0.0005[a]
Change in bodily pain	-1 (-7 to 6)	17 (7 to 27)	0.004[a]
Change in social function	-6 (-17 to 5)	19 (10 to 29)	0.003[a]
No. with emotional disorder[c] at baseline	26 (72%, 61% to 83%)	18 (60%, 48% to 72%)	0.3[b]
No. with emotional disorder[c] at follow- up	30 (83%, 67% to 93%)	12 (40%, 22% to 59%)	<0.0005[b]

a- student t-test
b- chi square test
c- emotional disorder is any of the following DSM IV diagnoses: major depressive disorder, minor depressive disorder, dysthymia, panic disorder, generalised anxiety disorder, anxiety disorder NOS as identified on the PRIME MD interview

records despite the patients having given permission. There were no cases where further assessment or investigation (by either GP or by other medical specialities) had uncovered an organic disease as an explanation for the presenting complaint.

10.5. Discussion.

Over half the patients who presented to neurologists with medically unexplained symptoms had not improved when they were reviewed eight months after their initial consultation. Patients' physical disability, ability to carry out work, pain symptoms, social function and mental health changed in line with their overall clinical outcome. No new cases of neurological disease were discovered during the follow-up period.

The only other study of the outcome of MUS in neurology patients discovered in the systematic review was by Jacobs and Russell (1961). They reviewed 92 consecutively presenting MUS patients five years after their initial presentation. They found that 33% were still symptomatic but they did not conduct any validated measures of health status or outcome. Their main concern was diagnostic accuracy and they were relieved to find that in only 5 cases was a previously undetected organic disease found which explained the presenting complaint.

These findings must be considered in the context of methodological shortcomings. The major concern is the loss of 24/90 (27%) of patients from follow-up. Although there is little evidence to suggest systematic bias, the outcome of the

patients who were not included in follow-up remains unknown. Nonetheless, even if it is assumed that all these patients fully recovered 40% of patients would have remained unchanged or worse and a further 17% improved but still symptomatic. Second, only 58 (64%) of General Practice case records were reviewed. Third, patients were not specifically subjected to a neurological examination at the time of follow-up.

Even with these limitations this data set allow the conclusion to be drawn that MUS are a cause of morbidity and distress to patients at the time of initial presentation but also that they remain so for around half of patients with them eight months later despite having had the benefit of a neurological consultation.

Randomised controlled trials have provided evidence that treatment for MUS can be beneficial. This includes structured management in primary care (Smith *et al* 1995), tricyclic antidepressant drugs (O'Malley *et al* 1999) and cognitive behavioural therapy (Kroenke and Swindle 2000). There is now an urgent need for large scale clinical effectiveness trials of these interventions.

Chapter 11. The outcome of depressive disorders in neurology patients.

11.1. Introduction.

Chapter 9 demonstrated a strong association between the presence of depressive disorders and decreased health status, including physical, social and work related functioning). The association was irrespective of whether the patients' symptoms were medically unexplained or as a result of neurological disease. However, what little evidence exists suggests that many of the cases of depressive disorder detected in general hospital in-patients remit spontaneously (Mayou and Hawton 1986). Additionally, it remains unclear whether remission of the depressive disorder will be associated with an improvement in health status. This chapter examines the eight months outcome of the 300 patients described chapter 9.

11.2. Aims.

Primary aim:

To determine how many patients had a depressive disorder eight months after their initial visit to the neurology clinic.

Secondary Aims:

i. To determine how many of those depressed at follow up had the depressive disorder at baseline assessment and in how many was it a new case?

ii. To determine whether a change in depression status (i.e. depressive disorder to no-depression or no-depression to depressive disorder) was associated with a change in functional status.

11.3 Analysis and justification of statistical techniques.

Analysis:

First, a comparison was made of the demographic and depression status results at baseline assessment between those who participated in follow-up and those who did not, in order to assess the possibility of systematic bias in the follow-up sample.

Second, demographic details and the presence of depressive disorders (major depressive disorder, partial remission of major depression, minor depression and dysthymia) in the follow up sample were described.

Third, the subgroup of patients who had a depressive disorder at baseline assessment were examined in order to determine the proportion who were still depressed at follow-up. The data on change in categorical depression diagnoses was supplemented with data on the change in total scores on the HAD scale between initial assessment and follow-up. Then the cohort were examined to determine how many new cases of depression had occurred and changes in the total HAD score of these cases were examined.

Fourth, in order to examine the association between change in depression status and functional status the changes in score on the SF-36 scales between baseline assessment and eight months follow-up were calculated for all patients. Then change in SF-36 scores between those patients whose depression status had changed and those patients whose status had remained the same were compared.

Finally, the cases of those patients who had recovered from depression were examined in order to address the question of whether it was the change in depression or neurological disease that had led to changes in health status.

11.4. Results.

Of the 300 patients assessed at baseline, 226 patients (75%) participated in follow-up, only those patients who participated in follow up are described in the outcome data. The sample followed-up comprised of 88 patients who initially had a depressive disorder (54 of whom had major depressive disorder), 17 patients who had an initial anxiety disorder but no depressive symptoms and 121 who had no initial psychiatric diagnosis.

There was no evidence of any systematic bias by sex or depression status in those who participated at follow-up. Although those not participating were slightly more likely to be younger patients and to have major depressive disorder, the differences were neither substantive nor statistically significant (table 11.1).

At follow-up 98 of the 226 patients (43%) were found to have a depressive disorders (major depressive disorder, partial remission of major depression, minor depression and dysthymia). Sixty six out of 226 (29%) had major depressive disorder (table 11.2).

Table 11.1. **Comparison of baseline characteristics of sample who participated in follow up (n=226) and those who did not (n=74).**

	Followed-up	Not followed-up	chi-square[a]	p
Number	226	74		
mean age	43.4	39.75	-3.7 (-7.9 to 0.6)[b]	0.09[c]
number male	93 (41%)	33 (45%)	0.3	0.7
any depressive disorder	88 (39%)	31 (42%)	0.2	0.7
major depressive disorder	54 (24%)	23 (31%)	1.5	0.2
mean HAD score	11.5	11.7	0.3 (-1.8 to 2.3)[b]	0.8[c]

a- one degree of freedom.
b- difference in means with 95% confidence intervals.
c- student's t-test.

Table 11.2. **Psychiatric status for the whole sample at baseline and for the followed up sample at 8 months follow-up.**

	Initial assessment n=300	8 months follow-up n=226
any depressive disorder	119 (40%)	98 (43%)
depressed at initial assessment	-	69
anxiety disorder only at initial assessment	-	8
new case	-	21
major depressive disorder	77 (26%)	66 (29%)
depressed at initial assessment	-	46
anxiety disorder only at initial assessment	-	5
new case	-	15
mean HAD score	11.5	10.5

Of the 88/226 patients who had a depressive disorder at *initial* assessment, 69 (78%) still met DSMIV criteria for a depressive disorder at follow up. Recovery from a depressive disorder was associated with a mean decrease of 5.5 on the HAD scale total score. Of the 54 patients who had major depressive disorder at initial assessment 46 (85%) still had major depressive disorder at follow-up. Recovery from major depressive disorder was associated with a substantial mean decrease of 10.1 on the HAD scale total score.

Of the 138/226 patients not depressed at initial assessment 29 (21%) had developed depression by follow-up. Twenty (14%) of these patients met criteria for major depressive disorder.

Table 11.3 shows the comparison of mean changes in SF-36 scores between those patients who had major depressive disorder at baseline assessment but had recovered by the time of follow-up with those patients who remained depressed. It can be seen that the improvements in health status with recovery from major depressive disorder were substantial.

Table 11.4 shows comparisons of mean changes in SF-36 scores in those patients who developed major depressive disorder by the time of follow-up compared with those who remained emotionally well. The development of depression was associated with a substantial decline in health status.

Table 11.3. **Eight months follow up of those patients who had major depression at initial assessment showing changes in HAD score and health status by outcome of depressive disorders (data from follow-up sample n=226).**

	Major depression at follow-up	Not depressed at follow-up	difference in means	95% C.I.
	n=46	n=8		
Mean change in HAD score	1.1	-10.1	-9.0	4.8 to 13.2
Mean change in SF36 score[1]				
Physical function	-4.0	13.1	17.1	5.9 to 28.4
Physical role function	-2.2	46.9	49.0	12.3 to 85.8
Bodily pain	5.3	24.1	18.8	3.8 to 33.8
Social function	5.4	26.6	21.1	-3.3 to 45.6

[1] all scores on the SF-36 range from 0-100. A lower score indicates increased disability or more pain.

Table 11.4. **Eight months follow up of patients who were not depressed at baseline showing changes in HAD score and health status associated with development of major depressive disorder (data from follow-up sample n=226).**

	Major depressive disorder at follow up	Not depressed at follow-up	difference in means	95% C.I.
	n=20	n=118		
Mean change in HAD score	-7.3	1.4	8.7	6.1 to 11.4
Mean change in SF36 score[1]				
Physical function	-14.3	0.6	15.0	7.0 to 22.9
Physical role function	-20.0	3.1	23.1	3.7 to 42.4
Bodily pain	-3.9	4.9	8.9	-3.7 to 21.4
Social function	-19.2	1.0	20.1	6.0 to 34.3

[1] all scores on the SF-36 range from 0-100. A lower score indicates increased disability or more pain.

The improvements in health status following recovery from major depression do not distinguish whether the improvement was due to either recovery from depression or improvement in the neurological condition. Unfortunately, the number of patients involved (8) was to small to address this issue satisfactorily although inspection of the cases suggested that in the majority of cases the improvement in health status could not be readily attributed to improvement in neurological disease.

11.5 Discussion.

There was a point prevalence of approximately 40% for DSM IV depressive disorders among patients followed-up eight months after their initial appointment at general neurology out-patient clinics. This was similar to the point prevalence of depressive disorders at the time of baseline assessment. Over three-quarters of cases of depression diagnosed at initial assessment persisted at eight months follow-up. Twenty one percent of those who were well at baseline assessment had depression diagnosed at follow up, indicating that neurology out-patients are at high risk of developing depressive disorders.

Recovery from major depressive disorder was associated with substantial improvement in HAD score. Recovery from major depressive disorder was also associated with substantial improvement in overall health status.

There are few relevant studies with which to compare these findings. There are data from primary care settings that suggest that depressive disorders tend to

persist in the absence of treatment (Zung *et al* 1990). Similar findings have been described for depressive disorders co-morbid with specific neurological diseases such as Parkinson's disease (Brown *et al* 1988), stroke (Astrom *et al* 1993) and multiple sclerosis (Ron *et al* 1992). These findings lend support to the conclusion that depressive disorders in neurological patients tend to persist.

Lesperance *et al* (1996) investigating major depression before and after myocardial infarction reported a strikingly similar result to the one described in this study. They showed that 30 out of 179 (17%) psychiatrically well patients went on to develop major depression during the six months following a myocardial infarction. One can hypothesise therefore that patients with physical symptoms of all types are at especially high risk of developing depression.

It has been previously recognised that depression contributes to patient disability whether occurring on its own (Wells *et al* 1989), or co-morbid with coronary artery disease (Frasure-Smith *et al* 1995, Sullivan *et al* 1997), neurological disorders (chapter 9) and stroke (Parikh *et al* 1990), and in high-utilising patients in primary care (Katon *et al* 1990). The findings described in this chapter demonstrate that the remission of depression may be associated with improvement in overall health status and disability in patients with co-morbid neurological disease. Unfortunately, so few patients recovered that it is not possible to determine whether this improvement was explained solely by improvement in neurological condition, or whether improvement in depression also played a role. This issue is important as depression should be amenable to effective treatment.

The findings described must be interpreted in the context of methodological limitations. First, 74 patients, 31 of whom had depressive disorders, did not participate in follow-up assessment. It is not possible to comment on their outcome. Nonetheless, even if it is assumed that they all remitted the conclusion can be made that depressive disorders persist in the majority of patients. Furthermore, there was no suggestion that participation in follow-up was substantially biased by age, sex or initial mental state.

Secondly, as the majority of both initial and follow-up assessments were conducted by the author it was not possible for the second assessment of depression to be blind to patient status at initial assessment. Whilst this is a well recognised source of bias in treatment and aetiological studies, it is arguably less important in simple prognostic studies of this type, particularly as there was no prior expectation on the persistence of depressive disorders. Of note, findings from the self-report measure (HAD), were consistent with those from the interview measure (PRIME-MD).

This chapter has demonstrated that the majority of depressive disorders detected in a neurology outpatient setting persist at eight months. Furthermore, the rate of new depressive disorders during the follow up period was substantial. Resolution of depressive disorders, particularly major depressive disorder, was associated with an improvement in health status, and although the numbers were too small for statistical analysis, not readily attributable to improvement in neurological condition. There is therefore an urgent need to establish whether interventions to

treat depression would also improve health status in this sample. Such interventions may be of particular importance in neurological practice where many diseases are chronic and lack specific treatments.

Chapter 12. What health care resources have patients identified with medically unexplained symptoms in neurology used?

12.1 Introduction.

The cross-sectional study described in Chapter 8 demonstrated that patients with MUS account for 30% of new neurology out-patient contacts and the follow-up described in Chapter 10, despite its limitations, found that over half of these patients will be chronically symptomatic. Anecdotal evidence suggests such patients will be high utilisers of health service resources but the systematic review (Chapter 7.5) found little data to confirm this. Of the two studies found which examined health service contacts (Mace and Trimble 1996, Binzer and Kullgren 1998), both found similar rates of contact with primary care: mean number of visits per annum 7.9 and 6.7 respectively. Furthermore Mace and Trimbles' data suggests a heavy skew with a small number of patients being very high users of resources indeed.

This chapter describes the results of an examination of the primary care case records of the 66 patients with symptoms which were *not at all* or *somewhat* medically explained who participated in the follow up study (Chapter 10).

12.2 Aims

Primary aim:

To estimate the lifetime use of health care resources by neurological out-patients with medically unexplained symptoms.

12.3 Analysis and justification of statistical techniques.

Analyses strategy:

This section of results examined only those subjects who were rated as having symptoms which were *not at all* or *somewhat* medically explained (n=90) at initial assessment and who participated in the follow up study (n=66).

The analysis was confined to a description of the ongoing treatments and previous lifetime health service utilisation. As the data was heavily skewed it was decided to describe the mean, as a measure of central tendency, and the range.

12.4 Results.

Of the 90 patients with symptoms which were *not at all* or *somewhat* medically explained at initial assessment, 66 (73%) participated in the follow-up assessment. The mean age of those who participated was 42, 62% were female. There were no substantive differences between those subjects that did and did not participate. Their clinical outcome is described in Chapter 10.

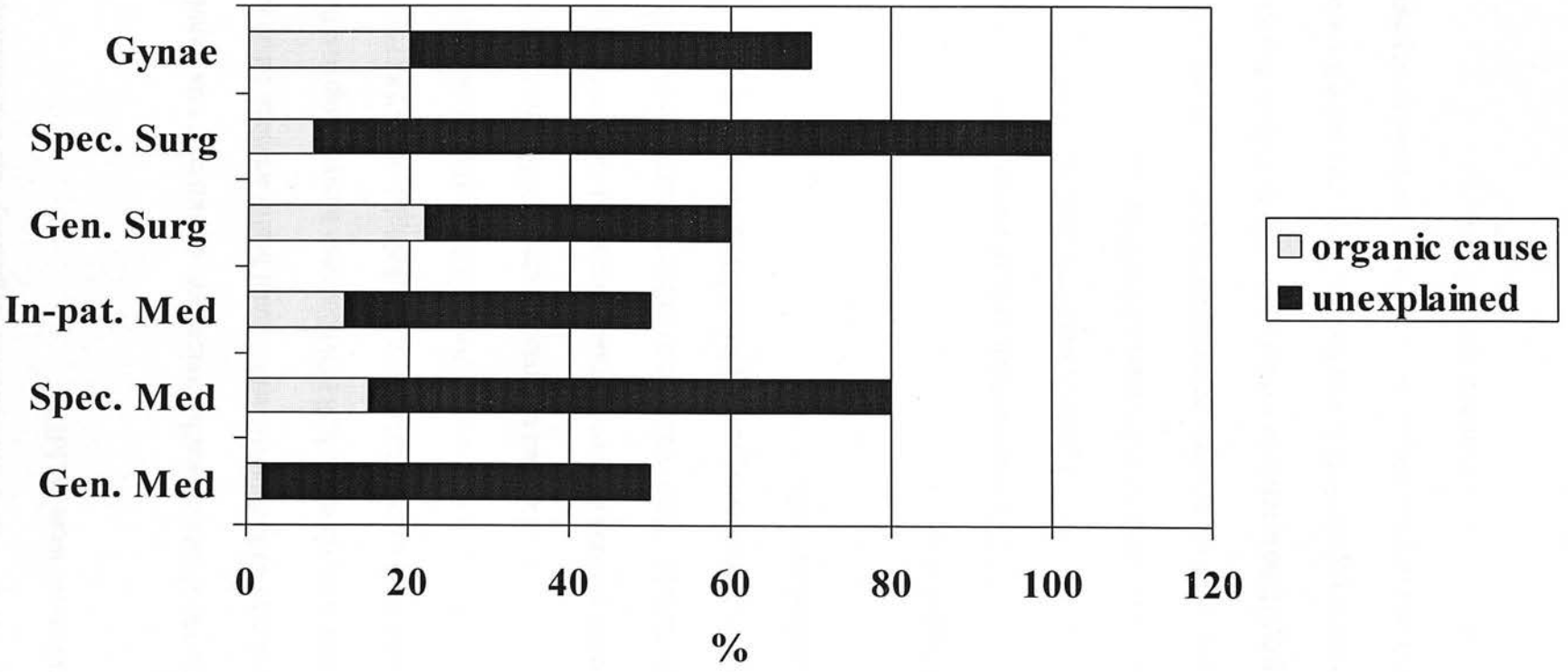
Review of the neurological case records was complete for all 66 patients. Review of the primary care records was only possible for 58/66 patients. In three cases the patients gave consent for follow up only and did not wish their general practice case records to be reviewed. In the other five cases the general practitioners refused permission to access the case records despite the patients having given permission.

The 58 patients whose notes were reviewed had had a lifetime mean of 96 general practice consultations (range 6 to 593), and a mean annual consultation rate of 7.5 consultations per year (range 1.6 to 197). Both figures are in keeping with population GP attendance rates in South-East Scotland (*www. ISD.gov.uk*). There was little change in the consultation rate after consulting with the neurologist: a mean decrease of 0.5 consultations in the six months following the appointment compared to the six months previous.

Only 17/58 (29%) of patients were not being prescribed medication. The mean was 2.3 regular medications per patient (range 0-10). Twenty two (22/58) patients were taking regular analgesics and 13/58 were taking regular psychotropic medication.

The rate of referral to other medical specialities appeared surprisingly high, particularly given the normal utilisation of primary care services. When only *new patient* clinic attendances were examined the median lifetime health service use was 3 new medical out-patient consultations (range 1-9), 1 medical in-patient stay (range 0-2), 3 new surgical out-patient consultations (range 0-10), 1 surgical in-patient stay (range 0-4), 2 accident and emergency consultations (range 0-6) and one mental health consultation (range 0-4). Figure 12.1 describes the percentage of patients who had at least one contact with medical/surgical specialities and

Figure 12.1 **Percentage of MUS patients who have had contact with another medical specialty (n=58)**



Spec Surg- includes orthopeadics, ENT and opthalmology

Spec Med- includes endocrinology, cardiology, and gastroenerology.

whether this was as a result of MUS or 'organic' disease. It can be seen that even using a conservative estimation of 'organicity' the overwhelming majority of the consultations were for MUS.

When use of mental health services was examined it was found that 32/58 (55%) of patients had had contact with mental health services. Seventeen (17/58; 29%) had seen a psychiatrist, 3/58 (6%) had seen a psychologist, a further 8/58 (14% had seen both a psychiatrist and a psychologist, and 4/58 (7%) had seen a community psychiatric nurse. Owing to the quality of the clinic letters it was difficult to estimate what treatments were actually offered but the impression was that most patients had one off assessments and the remainder had supportive psychotherapy. There was little to suggest accurate assessment and evidence based structured management plans. Unfortunately, this part of the data set must be regarded as weak.

12.5 Discussion.

Patients with MUS were not high users of primary care resources, although a very small number of MUS patients were very high users indeed with one patient making an average of 197 visits to her GP per year. The MUS patients had however received multiple referrals for specialist opinions. The overwhelming majority of those referrals were also as a result of MUS. Surprisingly, and contrary to popular belief, over half these patients had been seen by either a psychiatrist or psychologist (see Chapter 13) although it appeared unlikely that any evidence based treatments were offered.

The results on service utilisation found in this study are in keeping with those described by Trimble and Mace (1996) and by Binzer and Kullgren (1998). With all three studies suggesting normal use of primary care resources and a higher than anticipated use of secondary care resources. The results in this study are of interest as they confirm what the two earlier studies suspected, and show that the increased consultation rate is due to MUS, not separate unrelated organic disease. This was perhaps predictable given that the data in Chapter 8 showed that patients with MUS reported double the rate of somatic symptoms as patients with organic neurological disease. It seems likely that the main focus of attention switches between body symptoms over time.

These findings must be considered in the context of methodological shortcomings. The major concern is the loss of 32/90 (35%) of patients from follow-up and case note evaluation. Although there is little evidence to suggest systematic bias, the service utilisation of these patients remains unknown. Additionally the measure of health care utilisation was derived from case records and as such represents an estimate as prescriptions may have been unrecorded or specialist opinions mis-filed. Furthermore the recording of a consultation as being the result of MUS cannot be regarded as completely reliable. Although operationalised criteria were used and an attempt was made to be as conservative as possible in recording this data, it was nonetheless dependent on the quality of clinic letters which varied enormously. Similarly the high rate of psychiatric/ psychological consultation was completely unexpected and the data was inadequately collected leading to a lack

of information when it came to analysis. A final major limitation was that primary care records seldom covered a 'lifetime' and varied between records from birth to only the last two years. At the time of commencement of the study this was not realised and unfortunately no data allowing the calculation of a denominator was collected. This data should therefore be regarded as a current best estimate that undoubtedly requires further study.

Even accepting these limitations this data set do allow the conclusion to be drawn that not only are MUS a cause of morbidity and distress to patients but that they appear to be associated with a high utilisation rate of secondary, but not primary, care resources. This is perhaps not surprising as it is already known that patients present with MUS to all medical specialities. If waiting list times and removing pressure from secondary care resources are to remain a health service priority then strategic plans for the management of this group of patients may have to be the first step.

Chapter 13. How patients with medically unexplained symptoms were perceived.

13.1 Introduction.

All doctors recognise that some patients are harder to help than others. Over recent years a small literature has addressed what factors make a patient more 'difficult to help' (see table 13.3). These studies have mainly concentrated on primary care. The systematic review (chapter 7) did not discover any study that examined this question in neurology. This is of relevance as what represents a difficulty for a primary care doctor may not be a problem for a neurologist and vice versa. Nonetheless one factor that has been commonly associated with a patient being considered difficult to help in both primary and secondary care has been the presence of medically unexplained symptoms.

It is often said that patients with physical symptoms do not wish to be regarded as having 'psychiatric' disorders and there is compelling cultural evidence to support this (chapter 6.4). However, there is a surprising lack of empirical evidence on the views of the silent majority of patients who do not belong to politically active support groups or similar organisations.

13.2 Aims

Primary aim:

To determine whether neurologists found patients with medically unexplained symptoms more difficult to help.

Secondary Aims:

i. To determine patients' perceptions of need for psychiatric/psychological assessment or treatment.
ii. To determine general practitioners' perceptions of the need for their patients to have psychiatric/psychological assessment or treatment.
iii. To determine neurologists' perceptions of the need for their patients to have psychiatric/psychological assessment or treatment.

13.3 Analysis and justification of statistical techniques.

Analyses strategy:

First, the neurologists' *difficulty ratings* were compared across the four groups defined by their rating of the degree to which the patient's symptoms were medically unexplained. The non-parametric Kruskal-Wallis test was used as the data were not normally distributed. Confidence intervals were calculated using non-parametric techniques and appropriate tables (Gardner and Altman 1989).

Second, the neurologists' *difficulty rating* was dichotomised into *low difficulty* (Not at all difficult and Somewhat difficult) and *high difficulty* (Very difficult and Extremely difficult). A model was then constructed for multiple backward logistic regression. The model included the following variables: age, sex, organicity rating, SF-36 scores (physical function, physical role function, bodily pain and social function: the four mental health sub-scales were omitted as this variable was measured by PRIME MD and HAD), number of somatic symptoms, PRIME MD rating of (a) the presence of any DSM IV anxiety or depression diagnosis and

(b) the presence of major depressive disorder, and finally total HAD score. Age, SF-36 subscales and HAD total scores were converted into quintile ranges for the purpose of the regression analyses. The backward logistic regression analyses was conducted using SPSS software.

Then, to determine patients' perceptions of need for psychiatric/psychological assessment or treatment, the total sample was divided into four subgroups. First, the final scores from the neurologists' *organicity* rating were dichotomised into *neurological disease* (Largely explained and Completely explained) and *medically unexplained symptoms* (Not at all explained and Somewhat explained). These two groups were each further subdivided according to according to the presence or absence of a diagnosis of emotional disorder A comparison of the patients' ratings of need for psychiatric/psychological assessment or treatment was then made across the four groups. Confidence intervals were calculated using non-parametric techniques and tables (Gardner and Altman 1989).

This was repeated examining the GPs' and the neurologists' ratings of need for [the patient to have] psychiatric/psychological assessment or treatment.

Justification of statistical tests:

The use of Kruskall-Wallis test and confidence intervals have been described.

Multiple logistic regression is a more complex statistical technique based upon multiple linear regression. Unlike the Kruskall-Wallis and relative risk techniques,

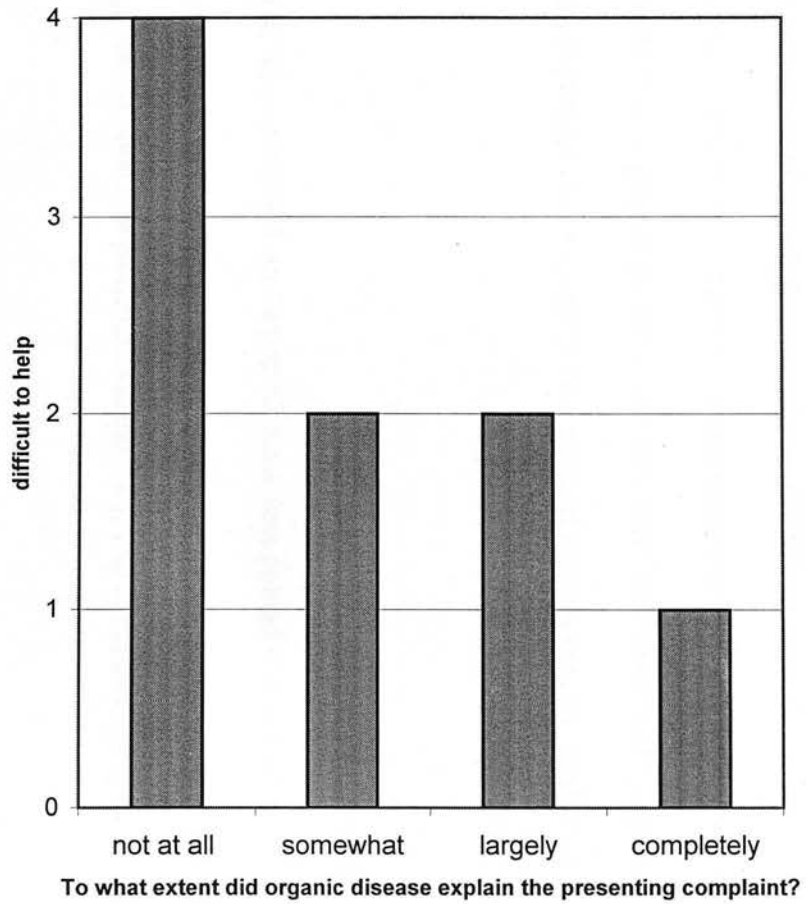
which only allow examination of two variables at a time, multiple linear regression yields a regression model in which the outcome variable is expressed as a combination of explanatory variables (co-variates). Multiple logistic regression follows the same principle but develops a model that uses a combination of the values of a group of explanatory variables to predict a transformation of the dependent variable. In this study this will be transformation from *low difficulty* to *high difficulty*. Such models are derived from multiple testing and as a result can be unreliable and over-optimistic with regard to the importance of each variable. To guard against this there are two oft used rules of thumb. One, is that there should be no more than n/10 variables entered into the equation, (in this study: 300/10= 30 variables for the model). The second is the square root of n as the maximum model size, (in this study: $\sqrt{300}$= 17 variables) (Gardner and Altman 1989).

13.4 Results.

Of the 300 patients, 143 were described as 'not at all difficult' to help, 111 were described as 'somewhat difficult', 27 as 'very difficult' and 18 as 'extremely difficult' to help.

When the scores on the neurologists' rating of 'difficulty rating' were compared across the four groups defined by the neurologists' rating of how medically explained the patients' symptoms were, those patients whose symptoms were poorly explained by organic disease were rated as more 'difficult to help' (Fig. 13.1).

fig 13.1. **Neurologists rating of difficulty by the extent to which the presenting complaint was explained by organic disease (n=300).**



The outcome of the backward logistic regression analyses is described in Table 13.1. It can be seen that the degree to which symptoms were medically explained was the main determinant of patients being perceived as "difficult to help". Additionally, the SF-36 physical function score also explained a small proportion of the variance. A model built from these two variables alone, correctly predicted difficulty in 86% of cases.

Table 13.2. demonstrates that few patients perceived any need for psychiatric/ psychological assessment or treatment. GPs and neurologists were more enthusiastic and it appeared they were guided by the presence of MUS rather than depression or anxiety disorders.

13.5 Discussion.

Neurologists' considered that patients with medically unexplained symptoms were more difficult to help. One other variable, physical disability, was associated with this perception but only explained a small amount of the variance. It is of note that age, sex, pain, number of physical symptoms and the presence of psychiatric diagnoses and number of physical symptoms did not influence the perception of the patient as being difficult to help.

Few patients expressed any interest in psychological/ psychiatric treatment and rather, they expressed their preference for a traditional medical approach. This was disappointing given the apparent importance of MUS and anxiety and depressive disorders demonstrated in the preceding chapters. Neurologists and

Table 13.1. **Stepwise backward multiple logistic regression analysis[1]- what makes a patient 'difficult to help'?**

Variable	B	S.E.	Wald	df	Sig	R	Exp (b)
symptoms were explained by organic disease	-1.087	0.177	37.614	1	0.000[2]	-0.375	0.337
Physical function	-0.227	0.125	3.275	1	0.070[3]	-0.071	0.797
constant	2.008	0.684	8.628	1	0.003		

[1] variables in model- age, sex, extent to which symptoms were explained by organic disease, SF-36 scores (physical function, physical role function, bodily pain and social function), number of somatic symptoms, PRIME MD ratings of (a) the presence of any DSM IV anxiety or depression diagnosis and (b) the presence of major depressive disorder, total HAD score.

[2] increased difficulty with symptoms which were poorly explained by organic disease.
[3] increased difficulty with poorer physical function

Table 13.2. **The number of patients requiring psychiatric/psychological treatment as perceived by the patients, the general practitioners and the neurologist (n=300)**
(% of total number in each column, 95%C.I.)

	Emotional Disorder		No emotional disorder	
	Unexplained symptoms N=60	**Neurological disease N=80**	**Unexplained symptoms N=30**	**Neurological disease N=130**
Patients pre-consultation	7 (12%, 5% to 23%)	5 (7%, 2% to 15%)	0 (0%, 0% to 12%)	1 (1%, 1% to 4%)
Patients post-consultation	8 (14%, 6% to 25%)	7 (9%, 4% to 18%)	0 (0%, 0% to 12%)	1 (1%, 1% to 4%)
General practitioners	20 (34%, 22% to 47%)	9 (12%, 6% to 22%)	9 (31%, 15% to 51%)	13 (10%, 6% to 16%)
Neurologists	33 (56%, 42% to 69%)	9 (12%, 6% to 22%)	7 (24%, 10% to 44%)	3 (2%, 1% to 7%)

general practitioners were more likely to consider the need for psychiatric/ psychological treatment. They were more likely to suggest this for those patients who MUS than those with neurological disease and co-morbid emotional disorders.

The systematic review failed to find any other studies that examine what factors cause neurologists to find a patient difficult to help. However, the question has been examined among primary care doctors in the United States (Lin *et al* 1991, Hahn *et al* 1996, Jackson and Kroenke 1999) and general medical and surgical consultants in the UK (Sharpe *et al* 1994) and among rheumatologists in the US (Walker *et al* 1997). The results of those studies are summarised in table 13.3. All these studies identified medically unexplained symptoms as an important contributory variable to the patient being perceived as difficult to help. In summary, doctors working in a variety of specialities find patients with symptoms they consider to be medically unexplained symptoms to be more difficult to help with their complaints than those in whom they can explain the symptoms by disease.

It is a commonly held belief, that many patients will not accept psychiatric input when they present to a general medical setting. The results found in this chapter seem to be in contrast with those reported in Chapter 12. One explanation for this is that few psychiatrists/psychologists actually know how to assess and treat a patient with unexplained symptoms, thus the limited contact served to reinforce

Table 13.3. **Factors associated with a patient being perceived as difficult to help.**

Study	Setting	Multivariate analysis	Age	Sex	Race	Social class	No. of symptoms	MUS	Mood	Pain	Illness behaviour	Physician experience	Patient satisfaction
Crutcher *et al* 1980	GP	-	+	-	-	+						+	
Deighton *et al* 1985	GP	+				+		+	+		+		+
Corney *et al* 1988	GP	-	+	+	-	-		+	+		+		+
Wright *et al* 1990	Paeds	-									+	+	+
Linn *et al* 1991	GP	+	-	-	-	-	+	++	+		+		
McDonald *et al* 1991	GP	-	-	-		+	+		+				
Hahn *et al* 1994	Med O.P.	+	-	-	-		-	++	+			-	
Sharpe *et al* 1994	Med O.P.	-	-	-				+	+		+		+
Hahn *et al* 1996	GP	+	-	-	-	-	+	++	+	+	+	-	+
Walker *et al* 1997	Rheum	+	-	-	-	-	-	++	-	-	+	-	-
Jackson *et al* 1999	GP	+	-	-	-	-	+	+	+		+		

- = no association
+ = association
++ = strong association

the patients view that there was no need for psychological treatment. Whilst the anecdotal evidence for this is believed by most in the field there appears to be only one other study of this in a neurological setting (Bridges and Goldberg 1984). They showed that half of patients wished their doctor to enquire about emotional symptoms. This referred to their treating neurologist and it is very possible that the number would have been much lower if they asked whether patients wanted referred to a psychiatrist to discuss their emotional problems.

These findings must be interpreted in the context of methodological limitations. The measurement of 'difficult to help' was made using a simple four point Likert scale rating which did not allow in depth exploration of what an individual neurologist actually meant when he or she rates 'difficulty'. Lothian neurologists may not be typical of neurologists elsewhere nor may their patients be typical although there is no reason to think that this is the case. Finally both the ratings of organicity and of difficulty were made at the same time. This does allow for the possibility of contamination. The rating of difficulty was the second of the two ratings to be made and would therefore be more susceptible to such an effect. However, one would assume that any contamination would be the result of a neurologist's view on treating patients with MUS (which is the point of the question) and thus distortion of results would be minimal.

Similar limitations apply to the measurement of the perceived need for psychiatric/psychological treatment. The measures were made on simple tick boxes and it is very possible this did not deal with the complexity of the issue. For

example many patients believe that psychiatric treatment equates with madness or purely disorders of emotions and they therefore perceive it as inappropriate as a strategy for managing their physical symptoms, whereas the same patients may gladly welcome a course of structured behaviour therapy aimed at symptom reduction.

Medically unexplained physical complaints are the single commonest reason for a patient to present to the health service. They account for 30% of neurology out-patient consultations (Chapter 8), affecting all ages, both sexes and are found in all cultures (Gureje *et al* 1997). What then should be done? Contrary to popular belief, there is good evidence that assessment and appropriate treatment leads to improved patient outcome (O'Malley *et al* 1999, Kroenke and Swindle 2000). It is in the interest of both doctors and patients, in terms of job satisfaction and consultation outcome, that all doctors should be trained in the basic skills of assessing and managing such symptoms. Even limited tuition has been found to improve doctors' self reported confidence in dealing with such patients (Jackson *et al* 1999).

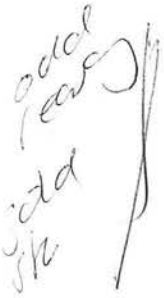
The lack of desire for psychiatric treatments is of serious concern, particularly since over of the half patients had had previous contact with psychiatric services. It would be easy to suggest that this is a matter for patient and doctor education but it maybe that a new approach is needed. Chapter 5 demonstrated that the way in which patients with MUS have been understood and managed has varied at different time in the history of medicine. Conceptualisations have changed and the

role of purely mental explanation waxed and waned. Treatment approaches have correspondingly changed from medical to psychological and back. Current evidence-based management includes both general aspects of medical care and specific 'psychiatric' treatments in the form of 'antidepressant' drugs and cognitive and behavioural therapies. However their 'psychiatric' implications make them often unacceptable to patients and physicians. All too often patients get caught between an excessively physical or excessively psychological approach. It may be necessary to consider a complete paradigm shift in which (a) unexplained complaints are re-medicalised around the notion of a functional disturbance of the nervous system and (b) treatments currently considered 'psychiatric' are integrated into the medical consultation (Sharpe and Carson 2001). Thus a predominantly physical model is given to patients but an emphasis is placed on the therapeutic benefits of psychological and particularly behavioural treatments.

This approach could incorporate the findings of recent research into the biological basis of such symptoms without losing psychological sophistication in management. The new paradigm would represent a return to a conceptualisation and form of management that was advocated 100 years ago by physicians such as Paul Dubois (1909), but now based on firmer evidence. This approach has the potential to revolutionise the clinical care that such patients receive and to make it acceptable to patients.

Chapter 14. Conclusions

This thesis aimed to examine the topic of medically unexplained symptoms in neurology by a combination of historical, narrative and systematic review of the literature and an original study of 300 newly referred patients to general neurology clinics in Edinburgh.



The historical review found that MUS are the oldest described medical conditions, although at that time paradoxically they had a completely physical explanation; a mobile uterus affecting other bodily parts. This hypothesis survived until the Renaissance when an increasing interest in first the brain and then the mind replaced the uterus as the organ of interest. The last 400 years have seen a constant oscillation between psychological and physical theories, modified by the general scientific milieu of the day, to explain these symptoms. To date no one has provided a satisfactory explanatory theory and these symptoms remain predominantly unexplained.

The narrative review of the literature showed that MUS affect all cultures, ages and both sexes. They are a cause of significant morbidity and disability to the world's health. There is strong evidence of an association with depressive syndromes. The exact nature of the relationship is unclear but the available evidence suggests that there is not a clear uni-directional causality. There is a spectrum of MUS severity and at the more severe end of the spectrum MUS tend to persist and be associated with markedly increased consumption of health care resources.

There are numerous aetiological theories and evidence to support both biological and psychological hypotheses. The symptoms are almost certainly multi-factorial in nature and social variables, such as litigation, do appear to be important as maintaining factors.

Although many doctors are pessimistic about the treatment of MUS there is in fact high quality evidence from randomised controlled trials (RCT) for specific treatments using antidepressants and cognitive behavioural psychotherapy. There is much less evidence about the non-specific aspects of treatment such reassurance and physical investigations, although there is RCT evidence supporting structured management in primary care.

The systematic review of MUS in neurology revealed a fairly consistent prevalence rate of between 30%-40% of patients having MUS. There was little quantitative data on disability. In the studies that examined the question there was an association with depression. Outcome studies were confined to studies on conversion disorder, with the exception of one retrospective study from 1961. There was no substantive evidence of high rates of missed organic disorders. Roughly half of the patients recovered spontaneously whilst the others remained symptomatic.

In the original study of 300 new referrals to neurology out-patient clinics, one third of patients had symptoms that were poorly explained by organic disease. The

patients with MUS had levels of disability comparable to those patients who had neurological disorders. Seventy percent of MUS patients had depressive or anxiety disorders. Depressive disorders were associated with increased levels of disability irrespective of whether a patient had MUS or neurological disease. One in eleven new patients attending neurological outpatient clinics had active suicidal ideation, major depressive disorder and MUS were the main risk factors.

Over half the patients who presented to neurologists with MUS had not improved 8 months later. The majority of depressive disorders detected in neurology outpatients persisted at eight-month follow up. The rate of new disorders was substantial. Resolution of major depressive disorder was associated with a reduction in disability. Neurologists found patients with MUS more difficult to help. Patients did not wish to have 'psychiatric/psychological' treatments for their symptoms.

In summary, medically unexplained symptoms affect one third of patients presenting to neurologists. They are the cause of significant disability and distress. They tend to persist in over half the cases. Although specific treatments exist they tend to be delivered in specialist centres. There is an urgent need for more research and greater emphasis on this group of patients in order that structured, effective clinical, management is available and can be delivered in a NHS setting.

Appendix 1. Acknowledgements

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- And most importantly of all Dr Michael Sharpe, Reader in Psychological Medicine, as a supervisor, colleague and friend.

Appendix 2. Publications related to this thesis.

Carson A.J., Ringbauer B., MacKenzie L., Warlow C. Sharpe M. (2000) Neurological disease, emotional disorder and disability: they are related. A study of 300 consecutive new referrals to neurology outpatient clinics. *Journal of Neurology Neurosurgery and Psychiatry* **68:** 202-206

Carson A.J., Ringbauer B., Stone J., MacKenzie L., Warlow C. Sharpe M. (2000) Do medically unexplained symptoms matter? A study of 300 consecutive new referrals to neurology outpatient clinics. *Journal of Neurology Neurosurgery and Psychiatry* **68:** 207-210

Carson A.J., Best S., Warlow C. Sharpe M. (2000) How common is suicidal ideation among neurology out-patients? *British Medical Journal*; **320:** 1311-1312.

Sharpe M., Carson AJ. (2000) Unexplained' somatic symptoms, functional syndromes and somatization: do we need a paradigm shift? *Archives of Internal Medicine.Annals of Internal Medicine* **134:** 926- 930.

Carson A.J., Postmas K. Warlow C. Sharpe M. A prospective cohort study of the outcome of depressive disorders in neurology patients. **In preparation.**

Carson A.J., Postmas K. Warlow C. Sharpe M The outcome of neurology patients with medically unexplained symptoms: a prospective study. **In preparation.**

Carson AJ, Warlow C, Sharpe M. (2000) Patients with medically unexplained symptoms are percieved as more difficult to help: a prospective study of neurological outpatients. **In preparation.**

Carson AJ, Stone J., Warlow C, Sharpe M. (2000) Medically unexplained symptoms in neurology patients: systematic review. **In preparation.**

Conference Abstracts:

Carson A.J., Ringbauer B., MacKenzie L., Warlow C. Sharpe M. (1999) Do medically unexplained symptoms matter? A study of 300 consecutive new referrals to neurology outpatient clinics. (Association of British Neurologists) *Journal of Neurology Neurosurgery and Psychiatry* supplement

Carson A.J., Ringbauer B., MacKenzie L., Warlow C. Sharpe M. (1998) Do medically unexplained symptoms matter? (European Conference on Psychosomatic Research) *Psychosomatic Research* supplement

Carson A.J., Warlow C., Sharpe M. (1999) Neurological disease, emotional disorder and disability: they are related. A study of 300 consecutive new referrals to neurology outpatient clinics. *Proceedings of the Royal College of Psychiatrists*

Carson A J.(1999) Proportions, associations and treatment of patients attending neurology clinics who have unexplained symptoms. (World Psychiatric Congress) *Current Opinion in Psychiatry* supplement

Carson A, Sharpe M, Warlow C (2000) Depressive Disorders in Neurology Out-Patients (Association of British Neurologists) *Journal of Neurology Neurosurgery and Psychiatry* supplement

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